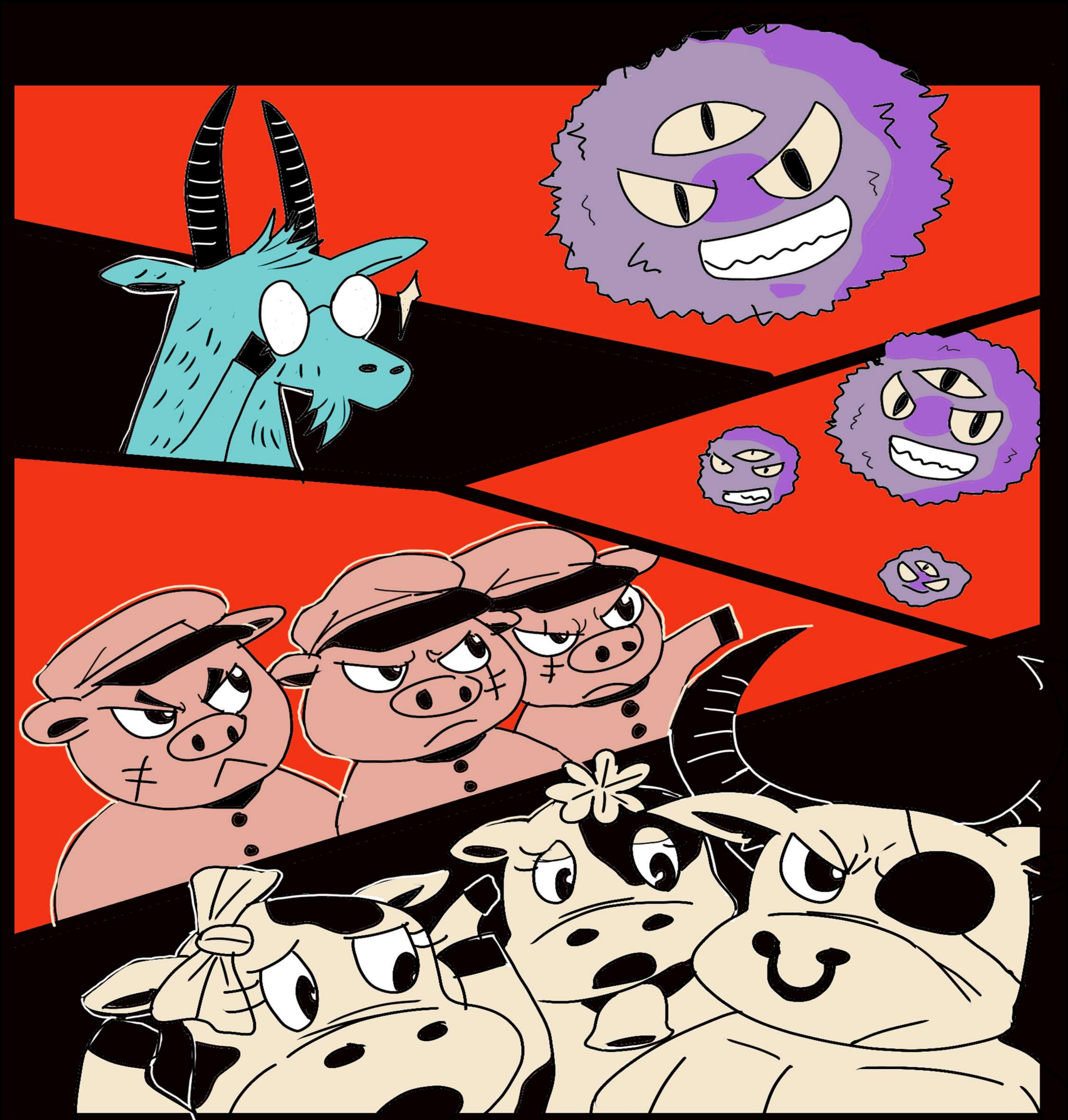
An integrated epidemiological and economic analysis of foot and mouth disease (FMD) in Thailand: Evaluation of FMD control measures



Thanicha Chanchaidechachai

Propositions

1. Data integrity is fundamental for planning foot-and-mouth-disease (FMD) control and surveillance in Thailand (this thesis).
2. The success of FMD control in Thailand is highly dependent on neighbouring countries' success in controlling FMD (this thesis).
3. The first step of modelling is to immerse oneself in the topic.
4. Networking is a key for interdisciplinary research.
5. Using social media and pop culture in science communication helps convey the scientific information to a broader audience.
6. Artificial intelligence is beneficial for jobs rather than a threat.
7. Graduating with a healthy mind and body requires not making the PhD the first priority in life.

Proposition belongs to the thesis, entitled

"An integrated epidemiological and economic analysis of
foot and mouth disease (FMD) in Thailand: Evaluation of FMD control"

Thanicha Chanchaidechachai
Wageningen, 4 October 2023

An integrated epidemiological and economic analysis of foot and mouth disease (FMD) in Thailand:

Evaluation of FMD control measures

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Table of contents


1

Chapter 1

General Introduction

1.1 **Background**

Overview of foot and mouth disease

Foot and mouth disease (FMD) is a contagious viral disease that affects multiple livestock species, such as cattle, pigs and small ruminants. Foot and mouth disease virus (FMDV) is an RNA virus of genus *Aphthovirus*, family *Piconarviridae.* It can be immunologically distinguished into 7 serotypes with no cross-immunity protection between serotypes, i.e., C, SAT1, SAT2, SAT3, O, A and Asia1 (Freimanis et al., 2016). The distribution of FMDV is different across the world. Africa, the Middle East and Asia are endemic areas, where serotypes O, A, SAT1 and SAT2 predominate in Africa, and serotypes O, A and Asia1 predominate in Asia. The other part of the world, such as Europe, America and some coastal islands of Asia, such as the Philippine, Taiwan and Japan, are FMD-free (Brito et al., 2017).

FMDV is highly contagious, and its morbidity can reach 100% in a naive population. The mortality is typically low in adults but can be high in young animals because of myocarditis. The incubation period from infection to clinical signs varies between 2 to 14 days (Davies, 2002). The common clinical signs include vesicles on the tongue, hoof, mouth and udder. The rupture of vesicles proceeds to ulcers resulting in lameness and loss of appetite due to soreness. Abortion might happen in pregnant animals because of high fever (Grubman & Baxt, 2004). During the acutely infectious period, the infected animals excrete the virus with expired air, blister fluid, saliva, milk, urine, faeces and semen. Susceptible animals can become infected by inhaling infectious aerosols, ingesting contaminated milk, being inseminated with contaminated semen, or coming into direct contact with contaminated fomites (World Organisation for Animal Health [WOAH], 2021b). Long-distance airborne spread can potentially happen in the temperate zone (Gloster et al., 2005).

All cloven-hoofed animals are susceptible to FMDV infection. However, the severity and transmissibility vary in different animal species. Cattle are highly susceptible to FMD, especially via the infection through the aerosol route. However, the disease is less obvious in the indigenous cattle breed from FMD-endemic areas, such as Asia and Africa (Kitching, 2002). FMDV can persist in basal epithelial cells of the pharynx and soft palate after recovery, and the recovered cattle might become a carrier that shed the virus for a year

(Salt, 1993). Pigs are considered to be amplifying hosts for FMDV since the infected pigs produce a huge load of aerosol virus compared to other species (Kitching & Alexandersens, 2002). FMD clinical signs in small ruminants are more transient, leading to difficulty in detecting the disease. Thus, the small ruminant can be hidden agents for FMD transmission (Kitching & Hughes, 2002). In Africa, wildlife such as wild buffaloes can serve as maintenance hosts that spread the disease to livestock (Thomson et al., 2003).

Global economic impacts of foot and mouth disease

FMD is regarded as the most important animal disease in terms of economic impact (James and Rushton, 2002). The economic impact of FMD is varied across countries due to the differences in FMD status, type of livestock, farming management and practices, and price of the inputs and outputs for livestock production (Rushton, 2008).

In FMD-free countries, the direct costs of an FMD outbreak include the cost of disease control measures and virus eradication (such as disease detection, pre-emptive culling, and vaccination), as well as the direct consequential costs of spread prevention and zoning (such as welfare slaughter and farm idle production). Moreover, there are also the indirect consequential costs of the market disruption during the outbreak (such as market disruption from domestic and international livestock trade bans and side-effect on non-livestock sectors) and the after-outbreak costs (such as the supply shock resulting from large-scale restocking and the cost of regaining FMD-free status) (Saatkamp et al., 2016). The total costs in FMD-free countries vary depending on the outbreak control measures and the severity of the outbreak. In the worst case, for example, during the FMD outbreak in the United Kingdom in 2001, the costs amounted to £3.1 billion in the agricultural sector, and the spillover effect on the tourism sector amounted to £2.7 billion (Thompson et al., 2002).

For the endemic countries, the costs of an FMD outbreak are more related to the production losses, which are more prominent in intensive dairy and pig farming than the extensive farming system (James and Rushton, 2002). The additional costs include the cost of control measures and vaccination. Knight-Jones & Rushton (2013) estimated that the losses in FMD-endemic countries all over the world approximately cost 7.6 billion USD for production loss and approximately 2.5 billion USD for vaccination. Apart from the monetary losses, it is worth noting that most FMD-endemic areas are developing countries where livestock is the main source of income and food for people. Thus, FMD can threaten the livelihood and food security of people in these areas (Perry and Rich, 2007).

Foot and mouth disease and its control in Thailand

FMD was first identified in Thailand in 1953 (Kehren & Tisdell, 1998). Since then, FMDV has circulated and caused outbreaks throughout Thailand. According to World Organisation for Animal Health (WAOH) report, 718 FMD outbreaks were reported throughout the country from 2017 to 2021 (WOAH, 2022a). Most of the outbreaks occurred in the central region, with cattle as the most affected specie. Serotype O is the most dominant serotype, followed by serotype A, while serotype Asia1 was last found in Thailand in 1998 (WOAH, 2016).

In 2008, the Department of Livestock Development (DLD) in Thailand launched the FMD national strategic plan (2008 – 2015) to control the FMD outbreaks. The main preventive measure was to achieve routine FMD vaccination coverage of more than 80% countrywide. Routine vaccination of ruminants is compulsory and fully supported by the government. The frequency of vaccination is 3 times per year in dairy cattle and 2 times per year in buffaloes, beef cattle and small ruminants. Routine vaccination of pigs is not mandatory, but the government supports vaccination efforts by subsidizing the cost of vaccines for pig farms. (Premashthira, 2018). Regarding the outbreak control measures, once the suspected cases or the outbreak are reported, the local DLD authority can announce the outbreak zone in their area of responsibility and implement the control measures, including quarantine of the infected premises, animal movement control, ring vaccination and environmental sanitary controls (Arjkumpa et al., 2020b; Yano et al., 2018).

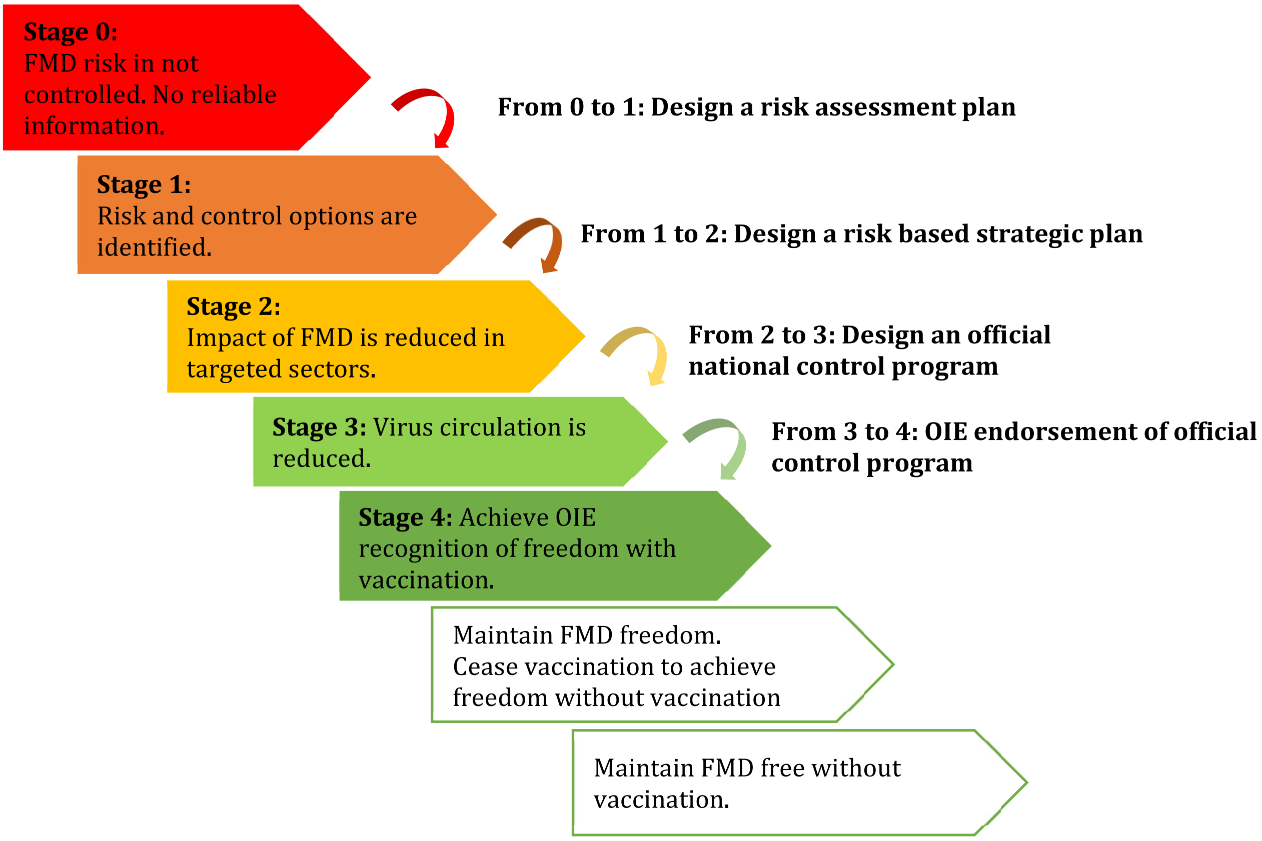

Figure 1.1 Progressive Control Pathway for foot and mouth disease (PCP-FMD) developed by Food and Agriculture Organisation of the United Nations (FAO) and World Organisation for Animal Health (WAOH) (FAO, 2018)

The national FMD control program in Thailand are established in accordance with the Progressive Control Pathway for foot and mouth disease (PCP-FMD). PCP-FMD is a risk-based framework developed by the Food and Agriculture Organisation of the United Nations (FAO) and WAOH to improve risk management and progressively reduce disease impact and prevalence in FMD-endemic countries (Food and Agriculture Organisation of the United Nations [FAO], 2018). The framework consists of 4 stages to reach the goal of official FMD-free status (Figure 1.1). Thailand is currently in an advanced stage 3 with an official control program endorsed by WAOH and working towards the FMD-free with vaccination status in the selected zones (WOAH, 2022b).

1.2 Problem statement

To maintain the current PCP-FMD stage and even aim further to FMD eradication in the selected zone, Thailand needs to strengthen control measures to progress in reducing disease incidence. Designing effective control measures requires understanding the epidemiology and economics of the disease in the areas. Knowledge of FMD epidemiology, such as the risk factors associated with the outbreak occurrence, the spatial and temporal pattern of outbreaks and the transmission dynamic of disease under different conditions, is fundamental to improving the control measures. Moreover, economic information, such as the FMD impact of disease on farms and the costs of control measures, is required to evaluate the economic feasibility of control measures. In the past decades, there have been numerous studies on the epidemiology of FMD in Thailand (Arjkumpa et al., 2020a; Chamnanpood et al., 1995; Cleland et al., 1996; Punyapornwithaya et al., 2022; Rojanasthien & Yano T, 2006; Sansamur et al., 2020) However, most studies were carried out in the regional level or mainly focused only the cattle, so far, the epidemiological research at the national level that can reflect the whole country's FMD situation is still lacking. Regarding the economic studies of FMD in Thailand, only a few studies on FMD economic impact on local dairy farms were presented (Laiya et al., 2020; Modethed et al., 2018; Panchakhan and Jintanawat, 2018). One study by Perry et al. (1999) evaluated the cost-benefit of FMD control program and eradication. To the best of our knowledge, no other studies on the economic assessment of FMD control measures in Thailand exist until now.

Modelling has frequently been utilised to offer information for the decision on FMD control strategies (Pomeroy et al., 2017). Since studies have shown that the transmission of FMD is linked with area characteristics, such as livestock species, farming system, and farm density (Backer et al., 2009; Boender et al., 2010; Keeling et al., 2001), the transmission model should take these factors into account to design control measures that are the best fit for the areas. These kinds of epidemiological models have developed in FMD-free countries (Backer et al., 2009; Ferguson et al., 2001a; Hayama et al., 2013; Keeling, 2005), but only a few models were built based on endemic areas (Belayneh et al., 2020; Jemberu, 2016a). So far, there is still a need for FMD transmission models in endemic areas that include area-specific factors, especially in Thailand, where such a model has never been developed before.

Besides the above-mentioned factors, the farmer's compliance is a critical factor that affects the success of control measures (Dürr et al., 2014; Jemberu et al., 2015). Most control measures were designed under the assumption that the implementation of control measures was perfectly executed, but in reality, the farmer's compliance is always less than perfect. Hence, it is important to consider the farmer's compliance when designing the measures.

With all mentioned knowledge gaps, the problems that hinder the improvement of FMD control measures in Thailand are the lack of epidemiological and economic information and the lack of model development to support the control decision. This thesis aims to fill these gaps by studying the epidemiology and economics of FMD in Thailand, inspecting the FMD transmission dynamic, developing the FMD transmission model based on real outbreak data and using the epidemiological and economic models to evaluate the FMD control with different compliance level.

1.3 **Objectives**

The overall objectives of this thesis are to gain epidemiology and economic information and to construct epidemiological and economic models based on this information in order to evaluate the control measures of FMD in Thailand. The results can help the local authorities design the appropriate control measures for their areas. The overall research objectives were broken down into five sub-objectives:

Analyse the spatial and temporal pattern of the FMD outbreaks and investigate the risk factors associated with the FMD outbreak occurrence at the country level.

I. Overview of the epidemiology of FMD outbreaks at the country level
II. Assess the FMD epidemiological and economic impact at the farm level
III. Study the transmission dynamic of FMD outbreak in the endemic area of Thailand
IV. Develop the FMD transmission model based on the inputs from real outbreaks and use this model to evaluate the consequences of control measures in different area conditions.
V. Evaluate the economic consequences of control measures by the integrated epidemiological and economic model

1.4 **Outline**

This thesis comprises seven chapters, including this general introduction (chapter 1), five research chapters (Chapters 2-6) addressing individual sub-objectives and a general discussion (chapter 7). Figure 1.2 shows a schematic overview of the thesis outline along with links between chapters.

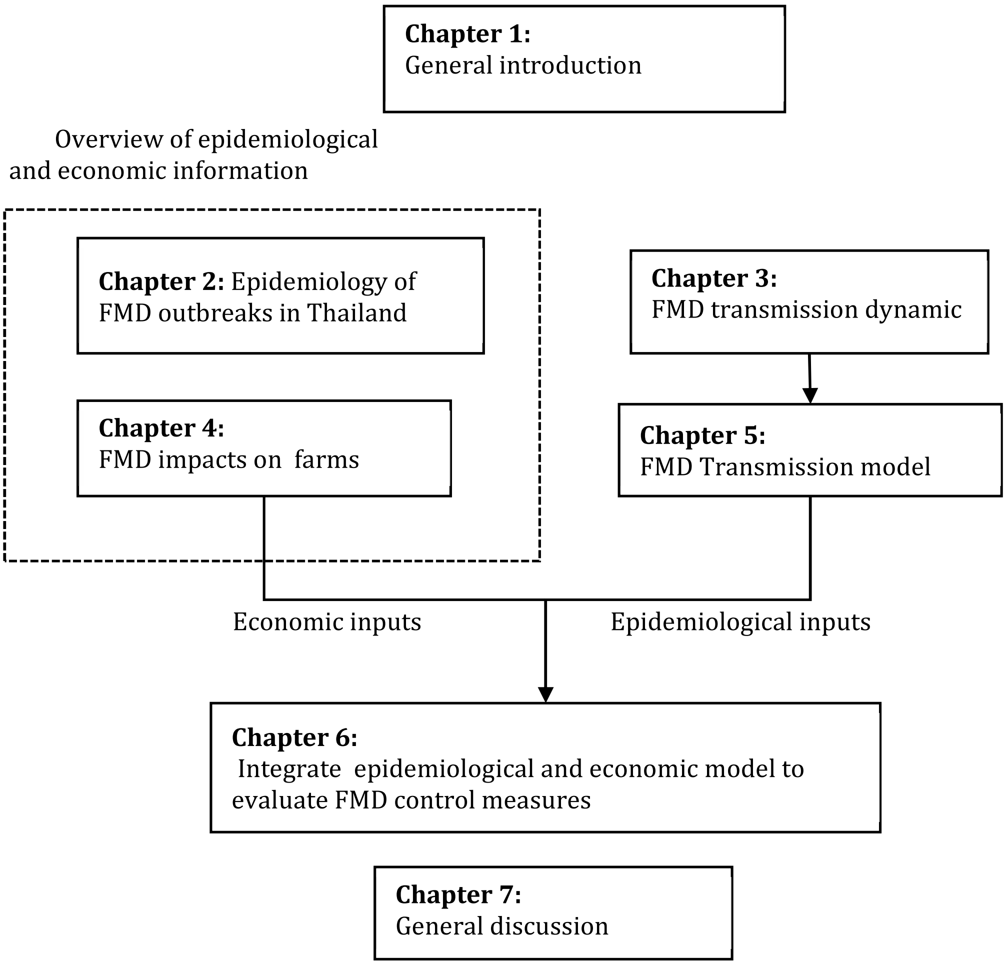

Figure 1.2 Schematic overview of thesis outline along with links between chapters

Chapter 2 describes the epidemiology of FMD at the national level using national FMD outbreak reports from 2011 to 2018. The spatial and temporal analysis was conducted to detect the high-risk areas and periods. The risk factors associated with FMD outbreak occurrence were identified. The results reflect a big picture of the FMD outbreaks in Thailand. Chapter 4 assesses the impacts of FMD on farms. Chapter 4 explores the FMD transmission dynamic based on local outbreak data and derives the transmission parameters. Chapter 5 develops an FMD transmission model to inspect outbreak consequences in the local endemic areas. Chapter 6 incorporates the economic model with the epidemiological model to evaluate the FMD control measures. The effect of farmer's compliance to the control measures was assessed.


2

Chapter 2

Epidemiology of foot and mouth disease outbreaks in Thailand from 2011 to 2018

This chapter is published as:
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Abstract

Foot and mouth Disease (FMD) is one of the most important animal diseases hindering livestock production in Thailand. In this study, a temporal and spatial analysis at the subdistrict level was performed on FMD outbreak reports in Thailand from 2011 to 2018. Risk factors associated with FMD outbreaks were furthermore investigated using generalized estimating equations. The results showed that the incidence of FMD outbreaks was the highest in 2016 and was affected by season, with a peak in FMD outbreaks occurring in the rainy-winter season from October to December. FMD outbreaks were mostly distributed in small clusters within a few subdistricts. Some high-risk areas with repeated outbreaks were detected in the central regions. Risk factors, including the increase in the subdistrict's size of the dairy population, beef population, or pig population, the low percentage of forest area, subdistricts in the provinces adjacent to Malaysia, the presence of a livestock market, and the occurrence of an FMD outbreak in a neighbouring subdistrict in the previous month significantly increased the odds of having an FMD outbreak. The increase in proximity to the nearest subdistrict with an FMD outbreak in the previous month decreased the odds of having FMD outbreaks. This study helped to identify high-risk areas and periods of FMD outbreaks in Thailand. Together with the identified risk factors, its results can be used to optimise the FMD control program in Thailand and in other countries having a similar livestock industry and FMD situation.

Keywords: foot and mouth disease, risk factors, spatial analysis, temporal analysis, Thailand

Introduction

Driven by domestic consumption and exports of animal products, livestock production in Thailand has been gradually growing since the late 1970s when farming systems in Thailand started to shift from extensive farming to intensive farming with an accompanying increase in farm size (Delgado et al., 2008). However, the growth of the country's livestock industry is hindered by multiple constraints, including infectious animal diseases, of which foot and mouth disease (FMD) is the most important in terms of economic impact (Perry et al., 1999).

Foot and mouth disease virus (FMDV) belongs to the Aphthovirus (family Picornaviridae) and can infect cloven-hoofed animals. FMDV consists of 7 immunologically distinct serotypes, O, A, C, Asia 1, SAT 1, SAT 2, and SAT 3 (Davies, 2002). Mainland Southeast Asia (SEA), which encompasses Peninsular Malaysia, Myanmar, Vietnam, Laos, Cambodia and Thailand, is endemic for serotypes O, A and Asia 1 (Knowles et al., 2012). Even with an annual vaccination program in place, 928 FMD outbreaks, distributed all over Thailand, have been reported to the ASEAN Regional Animal Health Information System from 2007 to 2017 (Blacksell et al., 2019). The risk of FMD outbreaks in Thailand has increased because of the increase in livestock trading in the SEA region due to a rise in livestock demand from China (Smith et al., 2015).

Area-specific knowledge of the epidemiology of FMD is fundamental to improving preventive measures and control strategies, as insight into the occurrence of FMD can help authorities allocate resources to areas at greater risk. Studies in a variety of FMD endemic areas showed multifaceted risk factors related to FMD, including the type of animal species (Nyaguthii et al., 2019; Yano et al., 2018), production system (Megersa et al., 2009), presence of a livestock market (Jemberu et al., 2016b), livestock traders (Souriya et al., 2020), adjacency to a national park (Allepuz et al., 2015), and a seasonal effect (Guerrini et al., 2019). Studies in SEA highlighted the importance of transboundary animal movement as the major risk of FMD transmission (Blacksell et al., 2019; Madin, 2011).

Most of the studies on FMD patterns and risk factors in Thailand were conducted at the regional level. For example, (Arjkumpa, Sansamur, et al., 2020) studied spatiotemporal clusters of FMD outbreaks in northern Thailand. A study focusing on

Northern Thailand dairy farms showed that farms located near communal grazing areas or slaughterhouses and imported cattle without quarantining animals were at greater risk for FMD (Sansamur et al., 2020). Another study by Sangrat et al. (2020) used experts' opinions to evaluate the weight of spatial risk factors associated with the occurrence of FMD in Thailand and used it to create a risk map. The authors found that the risk of FMD occurrences increased in areas close to a region with a previous outbreak, livestock markets, slaughterhouses, boundary lines, and areas with a high density of beef cattle, pigs, dairy cattle, buffaloes, humans, and roads (Sangrat et al., 2020). However, a study investigating the patterns and risk factors of FMD at the country level based on actual outbreak data is lacking. This study identified the spatial and temporal patterns of FMD outbreaks in Thailand and the associated risk factors based on subdistrict-level data of FMD outbreak reports from 2011 to 2018.

Materials and methods

Study area

Thailand is located in the middle of mainland SEA with an area of 513,120 km^2. The land border is adjacent to Myanmar, Laos, Cambodia and Malaysia. The administration structure consists of 77 provinces and subdivides into the local administration of districts (n = 878) and subdistricts (n = 7,425). The topographical features include a central plain, the upland plateau in the northeastern region, and the high mountains, which cover northern Thailand and extend along the Myanmar border to the Malaysia peninsula. The elevation varies from sea level up to 2,562 meters in the mountainous areas. The climate is divided into three seasons. The rainy season stretches from mid-May to mid-October. The winter season extends from mid-October to mid-February, during which most parts of the country experience dry weather with mild temperatures. Finally, the summer season stretches from mid-February to mid-May (Thai Meteorological Department, 2015).

Livestock species typically affected by FMD are cattle, buffalo, small ruminants and pigs. The geographical distribution of livestock in Thailand is diversified. The majority of pig farms and dairy farms are located in the central, western and eastern regions. Beef cattle and buffalo farms are concentrated in the northeastern region, whereas most small ruminant farms are located in the southern region of Thailand (Department of Livestock Development [DLD], 2020).

The main control measure of FMD in Thailand is routine vaccination. It is supported by the Thai government by distributing free-of-charge trivalent FMD vaccines (O, A and Asia1 serotypes) for dairy cattle and a bivalent FMD vaccine (O and A serotypes) for beef cattle, buffaloes and small ruminants. FMD vaccines are produced by the Bureau of Veterinary Biologics Pak Chong facility in Thailand, distributed to local veterinary offices and the dairy cooperative network, and then to individual farmers, local veterinary officers and private farm veterinarians who vaccinate the animals. Vaccination of ruminants is compulsory. Dairy cattle are vaccinated three times yearly, while small ruminants, beef cattle and buffalo are vaccinated twice a year (Arjkumpa et al., 2020b). The government also produces a trivalent FMD vaccine (O, A, and Asia 1 serotypes) for pigs. It is commercially available and sold at a below-market price due to government subsidy (Yano et al., 2018) but pig farmers can also use other commercially available FMD vaccines (unpublished data from FMD project (PRP 5905021280)). The vaccination program for pigs is voluntary and depends on the farmers' own willingness to participate.

The Thai FMD surveillance program consists of both active and passive surveillance components. Active surveillance includes routine visits to cattle farms by local veterinary officers and monitoring the FMD status of imported cattle. Passive surveillance means that farmers are expected to report FMD-suspected cases upon notification to local veterinary officers (Arjkumpa et al., 2020b). When FMD outbreaks are reported, control measures are immediately implemented in order to stop disease transmission, including the quarantining of suspected premises, outbreak area announcements, animal movement control, and ring vaccination (Yano et al., 2018).

Data collection

Subdistrict-level FMD outbreak data between 2011 and 2018 were acquired from the Department of Livestock Development (DLD). Recorded data consisted of the name of the subdistrict having the outbreak, the starting date of the outbreak, the population size, and the livestock species involved. The outbreaks were clinically diagnosed by local veterinary officers, with at least one animal in the area showing the typical signs of FMD, and confirmed by laboratory tests using ELISA, virus isolation, PCR, or a combination of those, at the Regional Reference Laboratory for Foot and Mouth Disease in South East Asia.

Data on putative subdistrict-level risk factors associated with FMD outbreaks were collected from various sources. The subdistrict level data of livestock population, consisting of species and population size, were obtained from livestock census data. Due to a lack of completeness, census data were only available in 2013, 2015 and 2018. Therefore, the 2013 census for the livestock population was used from 2011 to 2013. The 2015 census for livestock population was used from 2014 to 2016, and the 2018 census for livestock population was used from 2017 to 2018. Monthly rainfall in Thailand data between 2011 and 2018 was obtained from the National Oceanic and Atmospheric Administration. Data on elevation, forest area and adjacency to neighbour countries were extracted from the Thailand raster map using QGIS 3.4 (QGIS Development Team, 2020). Locations of livestock markets and slaughterhouses were obtained from DLD database (Department of Livestock Development (DLD), 2019).

Statistical analysis

Temporal analysis

Time series of monthly FMD outbreak reports were created. If a new outbreak in the same subdistrict was reported within 30 days, we counted them as one outbreak, and only the date of the first outbreak report was analysed. Seasonal and trend decomposition with locally estimated scatterplot smoothing (STL) was applied to analyse seasonal effects and trends. STL is a method to decompose time series into three additive components (trend, seasonality and remainder) using locally estimated scatterplot smoothing, which is the process of smoothing a regression curve to data points. The components can be written as follows:

$$Y_v = T_v + S_v + R_v \tag{2.1}$$

Where Y = the series value; T = the trend component; S = the seasonal component; R is the remainder at time v. Seasonal and trend decomposition with locally estimated scatterplot smoothing started with the outer loop by estimating the trend component and assigning a robustness weight to each data point. The weight depended on the size of the remainder, which reduced the effect of outliers. The trend was subtracted from the raw data to detrend the time series. Then, the detrended series was passed to the inner loop where the seasonal component was estimated using locally estimated scatterplot smoothing cycle subseries (for the yearly seasonal, there were 12 cycle subseries, i.e., January to December). The outer loop was iteratively updated with the new trend components estimated by subtracting the estimated seasonal component from the raw data. The new detrended series was passed to the inner loop again to update the seasonal component. The process continued until the setting number of cycles was reached. The variation that was not explained by the seasonal and trend components was considered the remainder (Cleveland et al., 1990). The remainders were checked for autocorrelation to ensure that no trend or seasonal effect was left in the remainders. The strength of the trend (F_{T}) and seasonal (F_{S}) component on time series can be measured by:

$$F_T = 1 - \frac{Var(R_v)}{Var(T_v + R_v)} \tag{2.2}$$

$$F_S = 1 - \frac{Var(R_v)}{Var(S_v + R_v)} \tag{2.3}$$

The measure of the strength of each component has a value between 0 and 1. A value close to 1 shows a strong effect (Hyndman and Athanasopoulus, 2018), while a value close to 0 indicates no effect from the component. The STL method was applied using the stl package in R program version 3.6 (R Core Team, 2022).

Spatial analysis

The spatial distribution of the risk of subdistricts experiencing an FMD outbreak was described by calculating standardised morbidity ratios (SMRs) at the subdistrict level for each year. SMR is the ratio of the observed number of cases relative to the expected number of cases in each subdistrict, where a case was defined as an animal with clinical signs of FMD. The expected cases for each subdistrict were calculated by multiplying the incidence rate from the entire population, which equals the total number of cases divided by the total population at risk, with the size of the population at risk in each subdistrict. If SMR > 1, the risk for that subdistrict is higher than the national risk. Therefore, SMR can be interpreted as a relative risk (Waller & Gotway, 2004). Estimated SMRs for areas with a low animal population may be imprecise because of variance instability. An empirical Bayes estimator with a Poisson-Gamma model was therefore applied to improve SMR estimates (Clayton & Kaldor, 1987). The number of years that subdistricts had SMRs > 1 was depicted in a choropleth map. The higher the number of years that subdistricts had SMRs > 1, the more likely these subdistricts were hot spot areas of FMD outbreaks. The heterogeneity of SMRs was assessed using a chi-square test. The global Moran's I index was used to quantify the spatial autocorrelation of SMRs. The null hypothesis is that SMRs are randomly distributed among the areas. A positive Moran's I index implies a clustering of high or low SMRs in the same neighbourhood area. A negative Moran's I index implies the dispersion of high or low SMRs (Bivand et al., 2013). Moran's I index can be calculated by

$$I = \frac{N\ \sum_i \sum_j w_{ij}(SMR_i - \overline{SMR})(SMR_j - \overline{SMR})}{(\sum_i \sum_j w_{ij})(SMR_i - \overline{SMR})} \tag{2.4}$$

Where N = the number of spatial units indexed by i and j; SMR_i = SMR for subdistrict i; SMR_j = SMR for subdistrict j; w_ij = the inverse of the distance between the centroid of subdistrict i and the centroid of subdistrict j (Gómez-Rubio et al., 2005). The spatial analyses were conducted for all years combined and each year separately and were performed in R program version 3.6 (R Core Team, 2022) using the DCluster package.

A discrete Poisson scan statistic was performed using SaTScan™ software, version 9.6 (Kulldorff, 2020) to detect the location of spatial clusters of FMD cases consisting of the number of animals with FMD. The centroid of subdistricts was assumed to represent the outbreak location. The subdistrict name, the number of animals with FMD, the animal population in each subdistrict, and the geographical coordinates of subdistrict centroids, were provided as input files. The expected number of FMD cases was calculated based on the animal population in each subdistrict using a Poisson distribution. Circular windows of varying sizes were then scanned over the space to find the clustering of FMD cases in the same area. Clusters of FMD were defined where the risk inside the window exceeded the risk outside the window. The likelihood ratio test was used to determine the most likely cluster. The *p* value is based on Monte Carlo hypothesis testing by comparing the maximum likelihood of actual data with randomly generated data (Kulldorff, 2018). The maximum spatial cluster size was set at 50% of the population at risk. The minimum spatial cluster size was set at more than 50 FMD cases to avoid cluster detection due to a small population at risk. The Gini index was used to select the reported clusters (Han et al., 2016), and clusters were not allowed to overlap. Only clusters with a significance level < 0.05 were reported. The scan statistics analysis was run for each year to remove the effect of long-term population structure changes. Subdistricts that had centroids located within significant yearly spatial clusters were reported in the maps.

Risk factor analysis

Generalized estimating equation (GEE) logistic regression models, to accommodate for autocorrelation of monthly reported data within subdistricts, were used to identify risk factors associated with FMD outbreaks. The dependent variable is the monthly occurrence of an FMD outbreak in each subdistrict. Putative subdistrict level risk factors included 1) the species-specific population size of livestock in each subdistrict i.e., dairy cattle, beef cattle, buffalo, small ruminants and pigs; 2) monthly rainfall; 3) elevation; 4) international border contact, defined as being a subdistrict located in a border province; 5) the presence of a slaughterhouse; 6) the presence of a livestock market; 7) a historical FMD outbreak in a neighbouring subdistrict in the previous month (a neighbouring subdistrict was defined as a subdistrict sharing adjacent borders to the subdistrict under scrutiny); 8) proximity to the nearest subdistrict with an FMD outbreak in the previous month; 9) the percentage of forest area, which is calculated by dividing the forest area by the total subdistrict area.

The year was included as a categorical variable in the model to correct the yearly trend in FMD outbreaks. The month was included as a sine-cosine function of the numerical month to present the seasonal fluctuation (Stolwijk et al., 1999). The basic statistical model can be written as follows:

$$ln\left(\frac{p}{1-p}\right) = \alpha + \beta_1 \times sin\left(2\pi \times \frac{m}{12}\right) + \beta_2 \times cos\left(2\pi \times \frac{m}{12}\right) \qquad (2.5)$$

Where p = the probability of having an FMD outbreak in a particular month; α = intercept; m = numerical month (1 to 12 for January to December). Due to the non-linear relationship between some independent variables and the log-odds of having an FMD outbreak, the continuous variables of the species-specific livestock population size and the proximity to the nearest subdistrict with FMD outbreak variables were log10-transformed. The percentage of the forest area and monthly rainfall were categorised based on three quantile densities. The exchangeable correlation structure was selected based on the lowest QIC of null models (Cui & Qian, 2007). Univariable analysis was performed for all putative risk factors. The risk factors with p value < 0.15 for the Type 3 test were eligible for the multivariable analysis. The correlation between the selected variables was checked. If the correlation coefficient was > 0.5, one of the correlated variables was selected. The correlation analysis showed a high correlation between elevation and the international border and between rainfall and the month of the year, which is not a surprise given that most mountainous ranges of Thailand stretch into neighbouring countries and the seasonality of rainfall. Since several studies showed that the international border is an important risk factor for FMD outbreaks, we kept the international border and month, while elevation and rainfall were excluded as the possible explanatory variables (Allepuz et al., 2015; Hamoonga et al., 2014; Picado et al., 2011). Subsequently, a backward selection process was applied to identify all variables significantly (p value < 0.05) associated with FMD outbreaks. The change of coefficient after dropping variables was checked to confirm that the dropping variables were not confounders. From the final statistical model, the predicted probability of having an FMD outbreak in the subdistrict for each month was calculated as follows:

$$probability\ of\ event = \frac{1}{1 + e^{-(\beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots)}} \tag{2.6}$$

The predicted probability was compared with the actual FMD outbreak report to visually evaluate the model fit when geographically being displayed on a map. We measured the correspondence between the predicted probabilities and outbreak incidences using Pearson correlation.

Results

Temporal analysis

From 2011 to 2018, 826 FMD outbreaks were reported. The monthly incidence of FMD outbreak reports is plotted in Figure 2.1. The median monthly incidence of FMD outbreak reports was 4 (min = 1, max = 81, mean = 9). The highest yearly incidence of FMD outbreak reports was in 2016 (n = 284), and the lowest was in 2011 and 2012 (n = 43). The decomposition plot is shown in Figure 2.2. As can be observed from the trend component, the incidence of FMD outbreaks increased from 2011 onwards and reached a peak in 2016 before decreasing. The seasonal component showed that the incidence of FMD outbreaks was low from February to June before increasing and reaching a peak from October - December. The measure of strength for the trend and seasonal components were 0.51 and 0.36, respectively, indicating that the effect of the trend component on the monthly incidence of FMD outbreak reports was more substantial than the effect of the seasonal component.

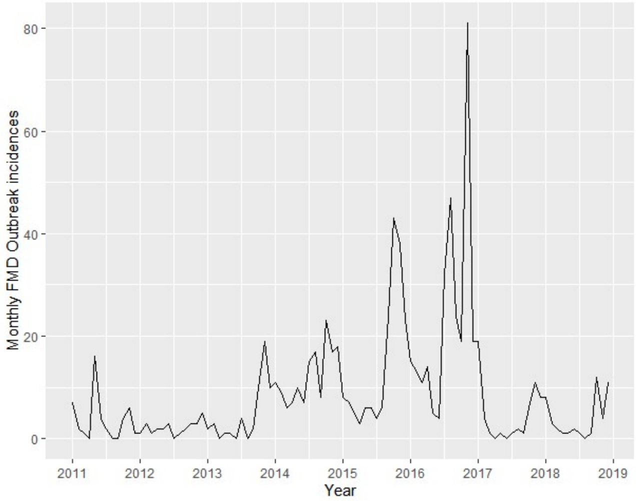

Figure 2.1 Monthly reported incidence of foot and mouth disease outbreaks in Thailand from 2011 to 2018.

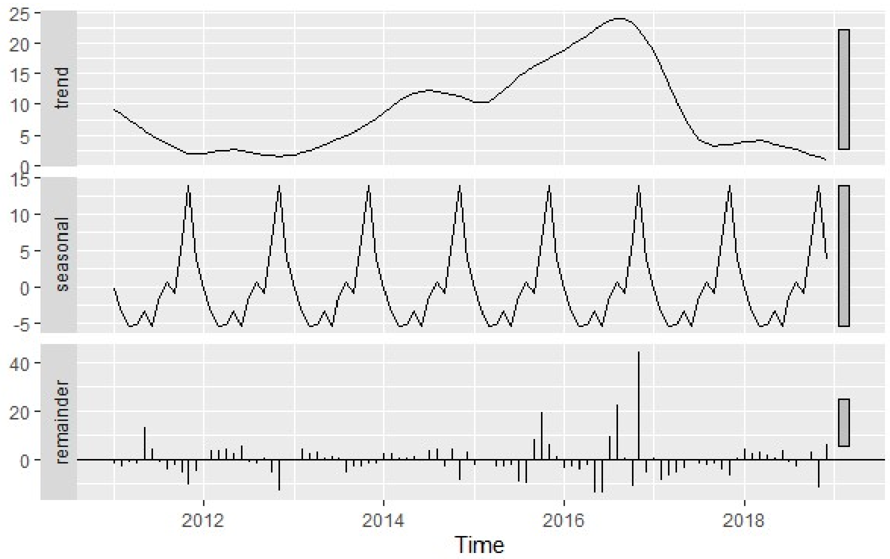

Figure 2.2 The decomposition of the monthly incidence of foot and mouth disease outbreaks in Thailand from 2011 to 2018 into a trend, seasonal and remainder component. The grey bars on the right side are scale bars of equal measurement, indicating the relative scale of each component.

Spatial analysis

Out of the 7,425 subdistricts in Thailand, 564 subdistricts reported at least one FMD outbreak. The subdistrict with the highest frequency of FMD outbreak reports was Lamphaya Klang subdistrict in Saraburi province, which is located in Central Thailand, with 12 FMD outbreaks reported from 2011 to 2018. The geographical distribution of subdistricts having SMRs > 1 is depicted on a choropleth map in Figure 2.3. The chi-square tests showed that the number of observed cases was different from the expected risk in some subdistricts (Table 2.1). Significant positive Moran's I indices were observed in 2011, 2012, 2013, 2016 and 2017 (Table 2.1), indicating clustering of high or low SMRs in the same neighbourhood area, although Moran's I indices values were low. The spatial clusters of similar SMRs in the same areas are depicted in Figure 2.4. Statistically significant spatial clusters were detected in 2011 – 2018. The reported clusters tended to be small clusters within a few subdistricts rather than large clusters. The clusters were mostly located in the central, southern and northern regions, except in 2016, when clusters were much more dispersed. The annual number of significant clusters varied from 8 clusters (year 2012) to 51 clusters (year 2016).

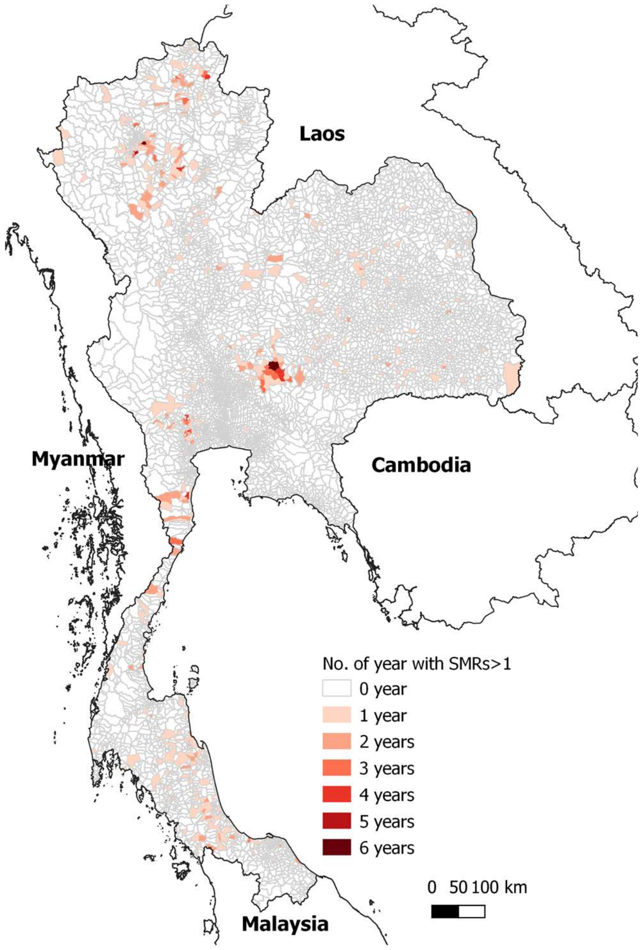

Figure 2.3 The number of years that subdistricts in Thailand had standardised morbidity ratios (SMRs) of foot and mouth disease outbreaks higher than one from 2011 to 2018.

Table 2.1 Presence of global spatial patterns of foot and mouth disease outbreaks in Thailand in 2011 until 2018 based on the chi-square test for the difference between expected risk and observed standardised morbidity ratios (SMRs) and the global Moran's I index

Year	Chi-square test	Moran's I index	Moran's I *p* value
2011	0.001	0.004	0.034
2012	0.001	0.03	0.001
2013	0.001	0.005	0.016
2014	0.001	0	0.291
2015	0.001	0	0.134
2016	0.001	0.037	0.001
2017	0.001	0.007	0.015
2018	0.001	0.002	0.098

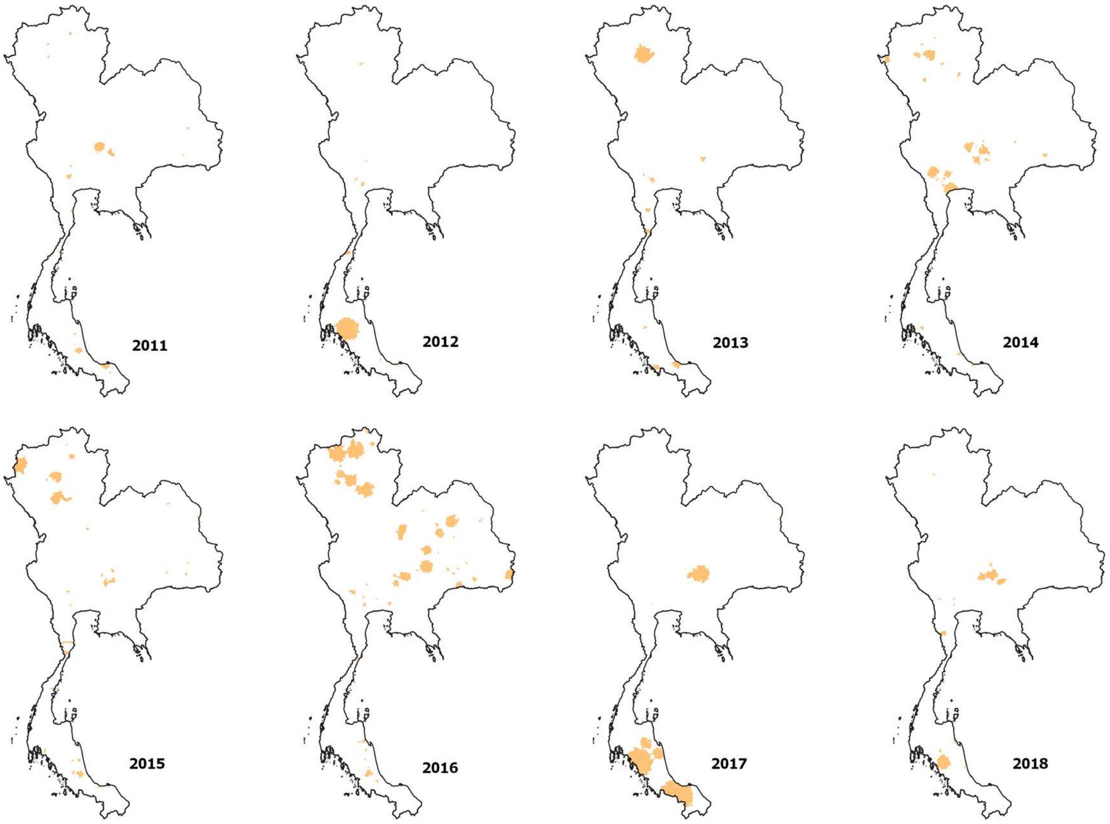

Figure 2.4 Locations of significant spatial clusters of foot and mouth disease outbreaks in Thailand from 2011 to 2018.

Risk factor analysis

Descriptive statistics of putative risk factors are shown in Tables 2.2 and 2.3. The distribution of the subdistrict had a high disparity for some risk factors. For example, there were relatively few subdistricts having a livestock market and a neighbouring subdistrict that experienced an FMD outbreak in the previous month. After correcting for seasonal and yearly trends, the final statistical model included eight statistically significant risk factors (Table 2.4).

Table 2.2 Mean and standard error of continuous risk factors for foot and mouth disease outbreak at the subdistrict level

Variable	Mean ± standard error	
	Subdistrict with FMD outbreaks	Subdistrict without FMD outbreaks
Log_{10} (dairy population)	1.49 ± 1.61	0.26 ± 0.71
Log_{10} (beef population)	2.75 ± 0.64	2.49 ± 0.78
Log_{10} (buffalo population)	1.10 ± 0.95	1.34 ± 1.05
Log_{10} (small ruminant population)	1.22 ± 1.18	0.70 ± 1.00
Log_{10} (pig population)	2.61 ± 1.13	2.16 ± 1.11
Log_{10} (proximity to the nearest subdistrict with the outbreak in the previous month)	2.05 ± 0.06	2.29 ± 1.01

Table 2.3 Descriptive analysis of putative categorical risk factors for foot and mouth disease outbreak at subdistrict-month level

Variable	Categories	No. of Subdistrict-month per categories (total n = 668,724)	FMD outbreak incidence per subdistrict-month
Monthly rainfall	< 50 mm	225,060	1.03×10^{-3}
	≥ 50 and < 180 mm	219,724	1.46×10^{-3}
	≥ 180 mm	223,940	1.21×10^{-3}
Elevation	< 36m	200,856	1.23×10^{-3}
	≥ 36 and <165 m	231,156	0.90×10^{-3}
	≥ 165 m	236,712	1.55×10^{-3}
Percentage of forest area	0%	552,576	1.18×10^{-3}
	> 0% and ≤ 33%	63,240	1.53×10^{-3}
	> 33% and ≤ 66%	36,552	1.67×10^{-3}
	> 66 %	16,356	0.79×10^{-3}
International border contact	No contact	412,608	1.15×10^{-3}
	Cambodia	67,260	0.46×10^{-3}
	Malaysia	28,428	1.86×10^{-3}
	Laos	91,104	0.97×10^{-3}
	Myanmar	69,324	2.57×10^{-3}
Presence of slaughterhouse	No	543,996	1.10×10^{-3}
	Yes	124,728	1.83×10^{-3}
Presence of livestock market	No	658,416	1.22×10^{-3}
	Yes	10,308	2.33×10^{-3}
FMD outbreaks in neighbouring subdistricts in the previous month	No	666,331	1.03×10^{-3}
	Yes	2,393	57.25×10^{-3}

Table 2.4 The final risk factor model for foot and mouth disease outbreak at subdistrict level with coefficients, standard error, odds ratio and statistical significance level

Variable	Coefficients	Standard error	Odds ratio (95%CI)	p value
Log$_{10}$ dairy population	0.72	0.04	2.06 (1.90 – 2.22)	< 0.001
Log$_{10}$ beef population	0.36	0.08	1.43 (1.22 - 1.67)	< 0.001
Log$_{10}$ pig population	0.20	0.04	1.22 (1.12 - 1.32)	< 0.001
Log$_{10}$ proximity to the nearest subdistrict with an outbreak in the previous month	-1.09	0.06	0.33 (0.30 - 0.38)	< 0.001
Percentage of forest area				
0% (none)	ref.			
> 0% and ≤ 33% (low)	0.25	0.13	1.29 (1.01 - 1.65)	0.04
> 33% and ≤ 66% (medium)	0.28	0.16	1.32 (0.96 - 1.81)	0.08
> 66 % (high)	0.008	0.27	1.01 (0.60 - 1.71)	0.98
International border contact				
No contact	ref.			
Cambodia	-0.43	0.20	0.65 (0.44 – 0.97)	0.03
Laos	0.29	0.15	1.33 (0.99 – 1.76)	0.05
Malaysia	0.96	0.18	2.61 (1.84 – 3.71)	< 0.001
Myanmar	-0.17	0.11	0.84 (0.68 – 1.03)	0.11
Presence of livestock market				
No	ref.			
Yes	0.55	0.30	1.74 (0.96 – 3.16)	0.068
FMD outbreaks in neighbouring subdistricts in the previous month				
No	ref.			
Yes	1.48	0.13	4.41 (3.42 – 5.68)	< 0.001
Year				
2011	ref.			
2012	-0.43	0.25	0.65 (0.40 – 1.05)	0.08
2013	-0.06	0.21	0.94 (0.63 – 1.41)	0.77
2014	0.96	0.17	2.62 (1.87 – 3.67)	<0.001
2015	1.09	0.17	2.99 (2.15 – 4.14)	<0.001
2016	1.48	0.16	4.37 (3.19 – 5.99)	<0.001
2017	0.24	0.21	1.27 (0.85 – 1.91)	0.24
2018	0.07	0.22	1.07 (0.69 – 1.66)	0.75
Month				
$\sin\left(2\pi \times \frac{m}{12}\right)$	-0.38	0.05	-	<0.001
$\cos\left(2\pi \times \frac{m}{12}\right)$	0.44	0.05	-	<0.001

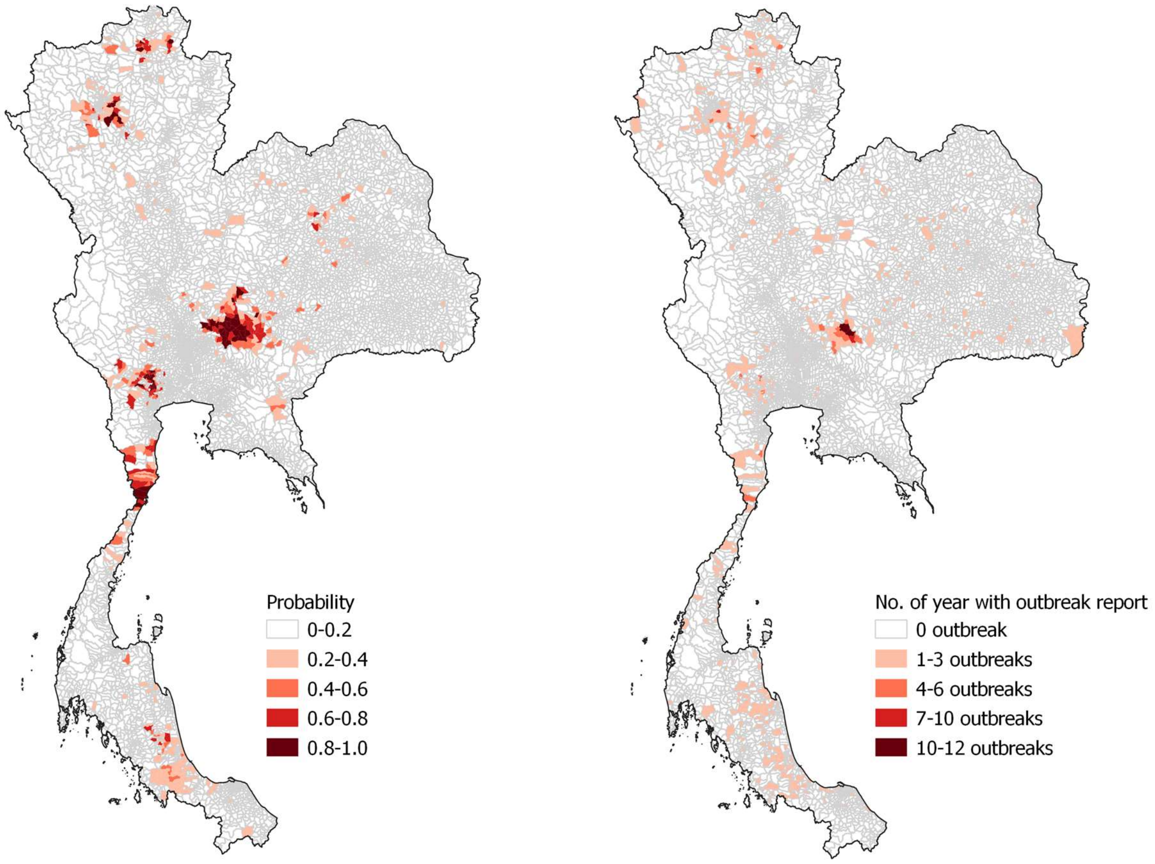

Figure 2.5 Geographical distribution of the predicted probability of foot and mouth disease outbreak resulting from the final statistical model (left) and the frequency of subdistrict-year level foot and mouth disease outbreak reports in Thailand from 2011 to 2018 (right).

A ten-fold increase in the population size of dairy cattle, beef cattle or pigs increased the odds of having FMD outbreaks 2.06, 1.43 or 1.22 times, respectively. The proximity to the nearest subdistrict with an FMD outbreak in the previous month was inversely related to the odds of having an FMD outbreak. A ten-fold closer proximity increased the odds of having FMD outbreaks 3 (=1/0.33) times. The areas with a low percentage of forest area had 1.29 times higher odds of having FMD outbreak than subdistricts without forests. Subdistricts located in the provinces neighbouring Malaysia had 2.61 times higher odds of FMD outbreak than the subdistricts located in provinces without international borders. Subdistricts having a neighbouring subdistrict with FMD outbreak in the previous month had 4.41 times higher odds of having an FMD outbreak compared to subdistricts not experiencing an FMD outbreak in any of their subdistricts in the previous month.

The predicted probability of having an FMD outbreak at the subdistrict level was compared with the actual FMD outbreak report (Figure 2.5). The high probability areas were mostly clustered in the central region and distributed as small patches in the north and southern part of Thailand. The predicted probabilities corresponded with the observed incidences with a Pearson correlation coefficient of 0.55.

Discussion

This study used reported outbreak data to describe the temporal and spatial distributions of FMD outbreaks in Thailand and to identify associated risk factors. It is one of the few studies conducted in FMD-endemic areas attempting to control the disease using vaccination. The number of FMD outbreaks was higher in 2016 than in other years, as indicated by the highest trend component in 2016. There is seasonal variation in the occurrence of FMD outbreaks, with the number of FMD outbreaks being the lowest in the summer season (March to May) and the highest in the rainy to winter season (October to November). The seasonal trend contradicts the results from previous studies in Africa, where the peak of FMD incidence occurred during the dry season because of increased animal movement to forage food and water sources (Ayebazibwe et al., 2010). However, livestock production in Thailand is more intensive and industrial, with livestock staying inside the farm areas without having a need to move around to forage for food, except for small beef cattle and buffalo farms. Another possible explanation is the effect of temperature and relative humidity on FMDV environmental survival. FMDV is expected to survive longer at low temperatures and higher relative humidity (Mielke and Garabed, 2020). This reason can explain a lower number of FMD outbreaks in dry summer and a peak in the rainy to the winter season when the temperature drops and the relative humidity remains high. Another possible explanation is a potential delay of vaccine delivery and vaccination practices in the rainy season, resulting in lower vaccination coverage, especially for smallholder farms in rural areas.

The results from the spatial analysis clearly showed that in some subdistricts, the incidence of FMD was higher than in other subdistricts. Certain regions are more vulnerable to the repetitive occurrence of FMD outbreaks, for which the risk factor analysis has provided some useful insights. The majority of FMD outbreaks tended to occur as small clusters within a few subdistricts rather than extending to a larger area.

The limited size of the FMD outbreaks might be explained by the immunity level in the population resulting from vaccination and the natural immunity from previous outbreaks (Pomeroy et al., 2015). An outbreak is self-limited when the population of susceptible animals in the area is depleted to the point that herd immunity is reached (Estrada et al., 2008).

The occurrence of outbreaks, despite a vaccination program being in place, implied a lack of herd immunity from the vaccination program. Several factors could be related to the vaccination inefficiency, such as a poor duration of vaccine-induced immunity (Knight-Jones et al., 2015), low matching of the vaccine with field strains (Mahapatra and Parida, 2018), and low vaccination coverage (Wataradee et al., 2021), especially in pig farms where the FMD vaccination program is not mandatory. The variation in FMDV strains might explain the high FMD incidence in 2016. The sequences of FMDV collected from FMD outbreaks in 2016 were classified as O/SEA/Mya-98 lineage, which differed from the sublineages Mya-98a that caused the FMD outbreaks in Thailand in 2009 (unpublished data from FMD project, Agricultural Research Development Agency, Thailand Thailand Research Fund (PRP 5905021280)). Moreover, a new strain – O/ME-SA/Ind-2001d was reported in 11 provinces of Thailand in 2016. The co-infection of FMDVs and intra-host recombination could increase the genetic diversity of FMDVs (Aiewsakun, Pamornchainavakul, & Inchaisri, 2020). Nevertheless, it is uncertain whether the outbreaks in Thailand result from ongoing transmission or from re-introductions from other locations. Further studies should be conducted to investigate why FMD outbreaks still occur in Thailand, even with vaccination.

The odds of FMD outbreak occurrence increased with the increasing size of the dairy cattle, beef cattle or pig populations in the subdistrict. Similarly, the size of the forest area was also a significant risk factor, which is a likely surrogate for farm density. These results were expected since a higher number of susceptible hosts may increase the chances of virus circulation. The varying odds amongst the different livestock species might be explained by the fact that different species vary in susceptibility and transmissibility of FMDV. Cattle are considered to be the most susceptible species, while pigs are the most infectious species (Bravo de Rueda et al., 2015). The occurrence of an FMD outbreak in a neighbouring subdistrict in the previous month and the proximity to the nearest outbreak were also significant factors. Both supported the possibility of an FMD outbreak through local transmission.

Previous studies suggested that transboundary transmission is a significant risk factor for FMD outbreaks in the Southeast Asia region (Blacksell et al., 2019; Smith et al., 2015). In our study, we found that subdistricts in provinces having international borders with Malaysia had a higher incidence of FMD outbreaks compared to subdistricts located in provinces not having an international border. Thailand is a transit country for large ruminants from Myanmar to higher-value markets in Malaysia via the southern borders (Wongsathapornchai et al., 2008b; Smith et al., 2015) and China via the northern provinces and subsequently the Laos-Vietnam route to China (Angkuraseranee et al., 2019; Bunmee et al., 2018). These international trade routes pose a risk for transboundary transmission. Despite the lower odds of FMD outbreak occurrence in the subdistricts of provinces bordering Myanmar and Cambodia, it is not possible to exclude the possibility of transboundary transmission between Thailand and these two countries. Due to an extensive amount of shared borders, a large number of ruminants are unofficially moved cross-border without taking appropriate biosecurity measures, such as quarantining or testing, leading to an increased risk of FMD transmission (Blacksell et al., 2019). The imported animals are typically transferred to animal markets or holding facilities for fattening in other areas (Smith et al., 2015). The studies on the link between animal movement networks and the occurrence of FMD in Thailand should be further conducted.

The results of the risk factor analysis were in accordance with a previous study from Thailand, based on expert opinion, suggesting that the risk of FMD occurrences would increase in areas located close to previous outbreaks, livestock markets, slaughterhouses, boundary lines, and areas with a high density of beef cattle, pigs, and dairy cattle (Sangrat et al., 2020). The current study supports these findings and quantifies the strength of the associations.

From the probability map, the majority of areas correctly predicted FMD outbreak occurrences, indicating a generally good fit of the model. However, we noted that some areas experienced FMD outbreaks while they had a zero probability of outbreaks, indicating that some underlying factors were not identified in our analysis.

Some potential limitations of this study should be considered. First, the FMD outbreak data in this study is based on the national reporting system, which is likely to be affected by reporting bias, as shown by several studies that the outbreak reporting underestimated the true prevalence (Siengsanan-Lamont and Blacksell, 2021; van Andel et al., 2020). In the areas that are susceptible to FMD introduction, such as international border areas and areas with a high number of farms, the local authorities might be more alert and conduct more active surveillance. Therefore, the outbreaks in these areas are more prone to be reported than in other areas. Passive surveillance, which depends on farmers reporting FMD cases, might cause under-reporting due to the concern over animal movement restrictions (Sangrat et al., 2020). Especially for pig farms, which are much more industrialised than ruminant farms, the economic impact of animal movement restrictions could be larger. Second, a case definition based on clinical diagnosis rather than on laboratory testing might further decrease the sensitivity of a report, especially if the infection happened in small ruminants, in which clinical signs are mild and inapparent (Bravo de Rueda et al., 2015). Third, we did not include animal density and the number of animal movements as potential risk factors in the analysis due to data availability. Still, these factors could be important and should be included in further studies. Fourth, the point geographical coordinates of each outbreak location were unknown. Therefore, the centroid of the subdistrict was taken to approximate the location of the FMD outbreak. The location might not represent the actual situation if the subdistrict is very large or if the outbreak involved multiple subdistricts. Despite those limitations, the available data are validated by reliable sources such as the Department of Livestock Development. The results are therefore expected to represent the actual outbreak situation in Thailand.

The results of this study can be used to improve the FMD control program in Thailand by helping authorities allocate resources and manage the control program more effectively. By focusing on areas and periods at greater risk of having FMD outbreaks resulting from ongoing, potentially undetected FMDV transmission, authorities can better prevent and control outbreaks. Vaccination efforts should be optimised in areas with high livestock populations, particularly in cattle and pigs cases. Like ruminants, pigs should have mandatory vaccination programs to improve vaccine coverage in the livestock population. To effectively select vaccine strains, it is suggested to sequence the virus more frequently and monitor changes in the circulating FMDV strains. Furthermore, vaccination should be performed before the start of the rainy season to ensure that animals develop immunity before the high-risk period. Since vaccination is performed by farmers in some areas, clear instructions should be given to ensure proper cold chain storage and vaccine administration. The potency and efficacy of the vaccine in the field should be monitored to ensure herd immunity. FMD awareness by farmers should be promoted to improve passive surveillance and uptake of vaccination. Concurrently, active surveillance of FMD should be planned for early detection and outbreak response.

Conclusions

FMD hinders livestock production in Thailand, as outbreaks have been occurring every year, despite routine vaccination and control programs. The occurrence of FMD outbreaks was affected by season and spatially clustered in certain areas with underlying risk factors. Risk factors associated with FMD outbreaks included the population size of certain livestock species, the size of the forest area, the international border, a history of an FMD outbreak in neighbouring subdistricts, the proximity to FMD outbreaks in a previous month and the presence of an animal market. The insight into the pattern and risk factors of FMD outbreak can help to manage resources in the high-risk areas and periods in Thailand.

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Supplementary materials

The programming code for models is available at:

https://doi.org/10.5281/zenodo.7708619


3

Chapter 3

Analysis of epidemiological and economic impacts of foot and mouth disease outbreaks in four district areas in Thailand

This chapter is published as:

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Abstract

Foot and mouth disease (FMD) is one of the most important infectious animal diseases impacting livestock production in Thailand. Despite a national vaccination program, FMD outbreaks are reported every year. We studied the epidemiological impacts of FMD outbreaks in four districts of Thailand between 2015 and 2016. Epidemiological data were collected from 193 FMD-affected dairy farms, 55 FMD-affected beef farms, and 25 FMD-affected pig farms. A significant difference in morbidity rate was observed between the dairy farms in the different areas, which could be explained by the differences in FMD outbreak management in each area. The morbidity rate in dairy and beef cattle also significantly differed between each animal age category, with the lowest morbidity rate observed in calves. Remarkably, vaccination was not significantly associated with the morbidity rate. In addition, the economic impact of FMD was calculated for 60 dairy farms in Muak Lek district. The economic losses were determined as the sum of milk production loss, mortality loss, additional labour costs, and veterinary service and medical costs, which averaged 56 USD per animal on the farm (ranging from 2 to 377 USD). Milk loss had the largest economic impact, although it varied substantially between farms. The farm size and outbreak duration were significantly associated with the total economic losses per farm. These results affirm the substantial epidemiological and economic impact of FMD on farms in Thailand, emphasizing the importance of FMD control.

Keywords: foot and mouth disease, economic, epidemiology, farm losses, morbidity, mortality

Introduction

Livestock production is an important economic activity in Thailand, contributing 12.6% of the country's gross agricultural production (Office of Agricultural Economics, 2020). The economic growth of Thailand and the increasing income per capita has led to a higher domestic demand for animal-derived food, while the demand from international markets such as China also drives the export of live animals and animal products (Smith et al., 2015). As demand increases, livestock farms in Thailand have grown and adopted more intensive farming practices (Poapongsakorn et al., 2003); however, this growth may intensify the risk and impacts of livestock diseases.

Foot and mouth disease (FMD) is a very important livestock disease in Thailand (Blacksell et al., 2019). This highly infectious viral disease affects cloven-hoofed animals, including pigs and large and small ruminants (Grubman & Baxt, 2004). Due to its high transmissibility, FMD is endemic in many parts of the world, including Africa, the Middle East, some parts of South America, and Asia, including Thailand (WOAH, 2021a).

The economic impact of FMD outbreaks in FMD-free countries is explicit. Enormous direct losses are related to eradication and indirect losses from closed export markets. By contrast, the economic impact of FMD in FMD-endemic countries is less clear, especially compared with other high-mortality animal diseases (Brown et al., 2021). The economic losses caused by FMD in its endemic areas have typically been estimated based on direct production losses, such as milk loss, mortality loss, and draft power loss (Barasa et al., 2008; Ferrari et al., 2014a; Senturk et al., 2008). Knight-Jones and Rushton proposed a framework for estimating the economic impact of FMD in endemic areas, defining the following factors: 1) visible losses due to milk loss and mortality loss; 2) invisible losses due to changes in herd structure and fertility problems; 3) additional costs due to control measures and treatment; and 4) revenue forgone due to loss of market access or the use of a suboptimal breed. The economic impact of FMD in the endemic regions of the world is estimated to be 6.5 to 21 billion USD per year (Knight-Jones & Rushton, 2013).

FMD is an endemic disease in Thailand, with regular reports of outbreaks all over the country. Between 2007 and 2017, 968 FMD outbreaks were reported in Thailand, especially between 2015 and 2016, when outbreak reports peaked at 183 (Blacksell et al., 2019). The FMD prevention strategies in Thailand include routine vaccination programs in ruminants two times per year or up to three times per year in areas with regular FMD outbreaks (Arjkumpa et al., 2020b). The government supports vaccination by providing free locally produced trivalent FMD vaccines (O, A, and Asia1 strains). Although the vaccination of ruminants is compulsory and supported by the government, the vaccination of pigs is voluntary, depending on the farmers. If an FMD outbreak occurs, the local authorities could respond by announcing the outbreak zone, enforcing emergency vaccination procedures, and applying animal movement restrictions within the outbreak zone (Yano et al., 2018). However, outbreak detection mostly depends on passive surveillance from farmer reports, and the intensity of outbreak management is at the local authority's discretion. In order to make good decisions, it is important for regional authorities to have insight into the epidemiological and economic consequences of an outbreak (Perry et al., 2001). Moreover, for farmers, an understanding of the consequences of FMD outbreaks is important when making decisions regarding the prevention and control of FMD.

Even though Thailand has been regularly affected by FMD, only a few epidemiological and economic assessment studies have been conducted. The previous studies mostly focused on the area level rather than the farm level (Arjkumpa et al., 2021; Sansamur et al., 2020). The knowledge gap of FMD impacts at the farm level in Thailand exists. This study, therefore, aims to explore the morbidity and mortality of FMD on dairy, beef, and pig farms using data from four FMD-affected districts, in addition to assessing the economic impact of FMD in dairy farms in Thailand.

Materials and methods

Data collection

Epidemiological data for FMD outbreaks between 2015 and 2016 were collected from four study districts in Thailand. These four study areas were selected from a consultation with Thailand's Department of Livestock Development (DLD) based on the criteria of a high density of livestock, differing structures of livestock farming, and the occurrence of FMD outbreaks between 2015 and 2016. The selected study areas were Muak Lek district, Bo Phloi district, Banpong district, and Mueang Lamphun district (Figure 3.1). These four districts are in different regions of Thailand and have distinct farm characteristics. Muak Lek district has the highest number of dairy cattle in Thailand, Bo Phloi district is predominated by beef cattle farms, and Banpong and Mueang Lamphun districts have a mix of dairy cattle farms, beef cattle farms, and pig farms (Department of Livestock Development, 2018).

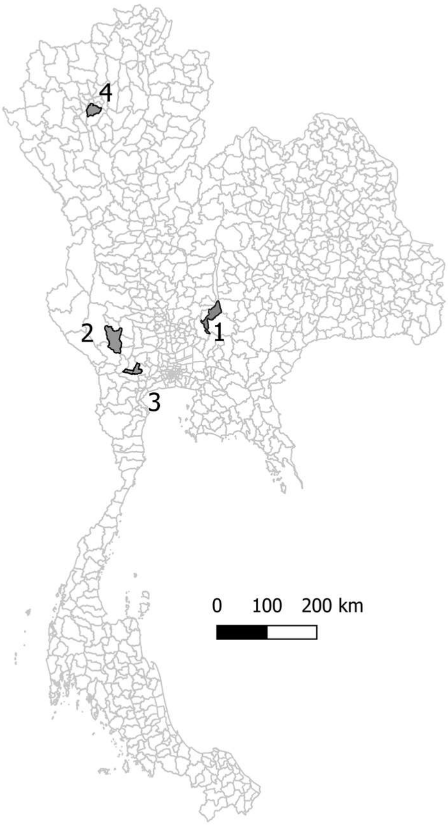

Figure 3.1 The study areas: (1) Muak Lek district, (2) Bo Phloi district, (3) Banpong district and (4) Mueang Lamphun district.

FMD-affected farms in the study areas were identified based on clinical signs by the local veterinary officers. For each FMD-affected farm, a farmer interview was conducted by local veterinary officers and research staff of the Veterinary Epidemiology and Animal Health Economics group of Chulalongkorn University, Bangkok, Thailand, using questionnaires in Thai. The staff were briefed on the questionnaires before the interviews started. The interview data consisted of the farmer's name, the geographical coordinates of the farm, the livestock species, the number of livestock, the outbreak start date, the outbreak end date, the vaccination practices, and the number of animals sick or dead with FMD symptoms in each animal category (defined by age and production status). Dairy cattle were categorised into calves (≤ 6 months old), heifers, and cows. Beef cattle were categorised into calves (≤ 6 months old) and adult cattle. Pigs were categorised into young pigs (suckling pigs and weaners), fattening pigs, and sows. FMD-affected animals were defined as animals that were sick or dead and showed clinical signs of FMD, i.e., lameness; drooling saliva; or vesicles on the udder, hoof, or tongue.

In addition, economic data were collected in Muak Lek district. Sixty FMD-affected dairy farmers from the epidemiological study were randomly selected to be interviewed about the economic impact of the FMD outbreak using an additional questionnaire. The economic data consisted of the reduction in milk production, milk price, outbreak duration, additional labour time, and the number of veterinarian visits. The interviews were conducted by the research staff. Additional economic data, including the prices of cattle, veterinary services, and medication, were estimated based on the expertise of local veterinarians and dairy cooperative staff, who were interviewed after the FMD outbreak (Table 3.1). The monetary data were collected in Thai baht prices and were converted to US dollars (USD) using the conversion rate of 1 USD to 35 Thai baht according to the average exchange rate in 2016.

Table 3.1 Input parameters for economic estimation in dairy cattle farms

Parameters (unit)	Notation	Value or calculation	Sources
Calf price (USD)	$Pcalf$	85.7	Experts
Heifer price (USD)	$Pheifer$	1,571.4	Experts
Wage rate (USD/ day)	W	8.6	Authors
Veterinary service fee (USD/animal/ visit)	vet	5.7	Experts
Average medicine cost (USD/ animal)	med	28.6	Experts

* 1 USD is approximated to 35 Thai Baht according to the average exchange rate in 2016

Epidemiological analysis

The overall cumulative incidence was calculated by dividing the total number of animals with clinical FMD signs by the total number of animals on the farm the day before the outbreak. This calculation was repeated for the cumulative incidence in each animal category, in which the number of sick animals with clinical FMD signs in each category was divided by the number of animals in the same category. The cumulative mortality was calculated in the same manner, using the number of dead animals that showed clinical FMD symptoms as the numerator.

A generalized linear model was used to study the effect of related factors on the count data of morbidity. The model was fitted separately for each animal species. The dependent variable was the number of sick animals with clinical FMD signs in each animal category for each farm. The log number of animals at risk was used as an offset to interpret the outcome as a morbidity rate. The independent variables were the study area, animal category, and FMD vaccination practice (≤ 1, 2, and ≥ 3 vaccinations per year). Due to the high turnover rate of animals in pig farms, the vaccination practices were based on the vaccination program in the sows. In addition, the study area was not included as an independent variable in the pig farm analysis since the number of infected pig farms in Mueang Lamphun district was very small (n = 2).

Due to the overdispersion of the data (the dispersion parameters in dairy cow = 4.8, beef cattle = 1.4 and pig = 55.5), a Poisson regression model could not be used, but generalized Poisson and negative binomial regression models were considered suitable alternatives (16, 17). The full model was fitted using both generalized Poisson and negative binomial regression and tested for zero-inflation using DHARMa package (Florian, 2017). If both models can handle the zero-inflation, the model with the lower Akaike information criterion (AIC) was chosen. After that, the stepwise backward selection process was conducted to choose the final model by excluding independent variables from the full nested model until the model with the lowest AIC was identified. The details on the model selection are shown in supplementary S2.

The mortality data were analyzed as a binary outcome (the absence/presence of dead animals with clinical FMD symptoms). A chi-square test was used to determine the statistical significance of the association between the presence of dead animals with FMD and the animal category or the vaccination practices. If the expected counts in the cell of the contingency table were below five, Fisher’s exact test was used instead (Shahbaba, 2012).

Estimation of economic impact

From the 60 dairy farms in Muak Lek district, the economic impact of FMD at each farm i was calculated as the sum of milk production loss ($Lmilk_{\mathrm{i}}$), mortality loss ($Lmort_{\mathrm{i}}$), additional labour cost ($Llabor_{\mathrm{i}}$), and veterinary service and medical costs ($Ltreat_{\mathrm{i}}$).

The milk production loss for each farm i, was estimated using the milk loss in animals that showed acute clinical FMD signs (Barasa et al., 2008):

$$Lmilk_i = NSlact_i \times ML_i \times D_i \times Pmilk \tag{3.1}$$

where $NSlact_\mathrm{i}$ is the number of FMD-affected lactating cows on farm i, ML_i is the average reduction in milk yield in kilogram (kg) per FMD-affected cow per day on farm i, D_i is the outbreak duration in days on farm i, and $Pmilk$ is the milk price.

The mortality loss in calves and heifers was based on the market price of the animals. The mortality loss in lactating cows and dry cows was calculated based on the cost of a replacement heifer adjusted with a depreciation factor reflecting the parity of the dead cows (Getaneh et al., 2017). According to the interview data, most farms did not sell the carcasses; therefore, potential revenues from selling the carcasses were not included in the calculation.

$$\begin{aligned} Lmort_i = {} & (NDcalf_i \times Pcalf) + (NDheifer_i \times Pheifer) \\ & + \quad \left[(NDlact_i + NDdry_i) \times Pheifer \times adj_{dairy}\right] \end{aligned} \tag{3.2}$$

where $NDcalf_\mathrm{i}$ is the number of dead calves on farm i, $Pcalf$ is the market price of a calf, $NDheifer_\mathrm{i}$ is the number of dead heifers on farm i, $Pheifer$ is the market price of a heifer, $NDlac_\mathrm{i}$ is the number of dead lactating cows on farm i, $NDdry_\mathrm{i}$ is the number of dead dry cows on farm i, and adj_dairy is the adjustment factor for a cow depreciation. Because data about the parity of the dead cows were not available, we set the adjustment factors as a median of 0.5.

During the outbreak, the farmers and household members spent extra time nursing the sick animals and managing the farms. The extra labour hours were converted to a monetary value for additional labour costs (Govindaraj et al., 2021).

$$Llabor_i = HL_i \times\ D_i \times W/8 \tag{3.3}$$

where HL_i is the extra labour hours per day during the outbreak on farm i, D_i is the outbreak duration on farm i, and W is the wage rate per day.

The veterinary service and medical costs were calculated as

$$Ltreat_i = (NS_i \times vet \times visit_i) +\ (NS_i \times med) \tag{3.4}$$

where NS_i is the number of sick animals on farm i, vet is the veterinary service cost per animal per visit, $visit_\mathrm{i}$ is the number of veterinarian visits on farm i during the outbreak, and med is the average medical cost per sick animal.

After calculating the economic losses, a linear regression model was fitted to identify the factors that were associated with the economic losses. The dependent variable was the total economic losses per farm. The independent variables were farm size, outbreak duration, and vaccination practice (≤ 1, 2, and ≥ 3 vaccinations per year). The final model was chosen by the lowest AIC. All statistical analyses were performed using R version 3.6 (R Core Team, 2022).

Results

Epidemiological analysis

Epidemiological data were collected from 193 FMD-affected dairy farms, 55 FMD-affected beef farms, and 25 FMD-affected pig farms in the four districts (Table 3.2). More than 75% of the farms vaccinated their animals at least twice per year, except for the beef cattle farms in Banpong district, of which only 21% vaccinated their animals at least twice per year.

Table 3.2 Number, species, herd size and vaccination of foot and mouth disease affected farms in the four studied districts with foot and mouth disease outbreak

Areas	Species	Number of FMD affected farms	Herd size Mean (Min, Median, Max)	Vaccination practices N (%)		
				≤ 1 per year	2 per year	≥ 3 per year
Muak Lek district	dairy	110	50 (7, 42, 160)	14 (12.7%)	20 (18.2%)	76 (69.1%)
Bo Phloi district	beef	26	81 (20, 56, 300)	5 (19.2%)	17 (65.4%)	4 (15.4%)
Banpong district	dairy	41	37 (8, 28, 118)	1 (2.4%)	14 (34.2%)	26 (63.4%)
	beef	29	32 (2, 20, 129)	23 (79.3%)	5 (17.2%)	1 (3.5%)
	pig	23	7,202 (115, 4,570, 30,000)	5 (21.7%)	5 (21.7%)	13 (56.6%)
Mueang Lamphun district	dairy	42	45 (5, 42, 130)	2 (4.8%)	6 (14.3%)	34 (80.9%)
	pig	2	67 (55, 67, 78)	0	2 (100%)	0

Table 3.3 Average percentage morbidity and mortality of each animal category in farms by areas

Species	Morbidity (%)				Mortality (%)			
	Muak Lek	Bo Phloi	Banpong	Mueang Lamphun	Muak Lek	Bo Phloi	Banpong	Mueang Lamphun
Dairy								
Calf	19.6	-	12.1	11.5	2.1	-	0	0
Heifer	29.4	-	34.3	24.1	0.9	-	0.3	0
Cow	49.6	-	31.4	17.8	0.7	-	0.6	0
Overall	41.1	-	33.0	16.5	1.0	-	0.5	0
Beef								
Calf	-	6.6	11.5	-	-	0	0	-
Adult	-	34.2	48.8	-	-	0	0	-
Overall	-	31.5	43.4	-	-	0	0	-
Pig								
Young	-	-	13.0	0	-	-	8.3	0
Sow	-	-	24.2	0	-	-	0.8	0
Fattener	-	-	35.1	12.6	-	-	4.9	0
Overall	-	-	33.4	4.7	-	-	5.6	0

"-" means no FMD outbreak report in this animal species in this district.

The cumulative incidence and cumulative mortality for each animal category are given as percentages in Table 3.3. The cumulative incidence varied substantially between the districts and animal categories. For the dairy cattle farms, the highest overall cumulative incidence and cumulative mortality were found in Muak Lek district, with cows having the highest cumulative incidence and calves having the lowest. For beef cattle farms, the overall cumulative incidence in Banpong district was higher than in Bo Phloi district, with adult cattle facing a higher cumulative incidence than calves. For pig farms, the overall cumulative incidence in Banpong district was higher than the overall cumulative incidence in Mueang Lamphun district; fattening pigs had the highest cumulative incidence.

The morbidity rate ratio, confidence interval, and significance value from the best-fit models are shown in Table 3.4. For the dairy farm, the morbidity rates in Banpong district and Muak Lek district were 1.22 and 1.97 times higher, respectively, than the morbidity rate in Mueang Lamphun district. In addition, the morbidity rates in the heifer and cow groups were 1.86 and 2.43 times higher than in the calf group, respectively. For the beef cattle farms, we did not find a significant difference in morbidity rates between outbreak areas; however, we did find that the morbidity rate in the adult cattle category was 4.09 times higher than in the calf group. For the pig farms, we did not see any statistically significant associations between morbidity rates and independent variables.

Table 3.4 Morbidity rate ratio, confidence interval and significance value from the best-fit models

Species	Variables	Rate ratio	95%CI	*p* value
Dairy cattle	Areas			
	Mueang Lamphun	Ref.		
	Banpong	1.22	0.90 – 1.64	0.197
	Muak Lek	1.97	1.57 – 2.49	<0.001
	Animal categories			
	Calf	Ref.		
	Heifer	1.86	1.34 – 2.60	<0.001
	Cow	2.43	1.80 – 3.28	<0.001
Beef cattle	Animal categories			
	Calf	Ref.		
	Adult	4.09	2.25 – 7.40	<0.001

Mortality from FMD was not observed in dairy farms in Mueang Lamphun district, and the overall cumulative mortality in the other three districts were less than 1%. The mortality in beef cattle farms was not calculated because only one dead calf was reported on a farm in Bo Phloi district. No mortality was reported in the two FMD-affected pig farms in Mueang Lamphun districts. Fisher's exact tests revealed no significant associations between the presence of animals that died with FMD and the related factors of animal category or vaccination practices.

Economic impacts

The economic losses were calculated for 60 FMD-affected dairy cattle farms in Muak Lek district (Table 3.5). The average total economic losses per animal were 56 USD, with a range of 2–377 USD per animal. The mean daily milk loss per animal varied substantially, with a range of 0.7–17.4 kg per cow per day. Consequently, the average milk losses per farm were 1,063 USD, with a range of 6–14,688 USD per farm. The average mortality losses per farm were 532 USD, with a range of 0–6,286 USD per farm. The highest economic losses per animal were due to milk production loss, which was, on average, 19 USD per animal, followed by mortality loss which on average, 18 USD per animal.

Linear regression was used to study the association between the total economic losses per farm and the putative influencing factors, including farm size, vaccination practice, and outbreak duration. Due to the big range of total economic losses per farm, we used the natural-logarithm transformation of total economic losses per farm as a dependent variable. Farm size and outbreak duration were found to significantly influence the log-transformed total economic losses of the farms (Table 3.6). For every one animal increase in the farm, the FMD total economic losses per farm increase 4.5% (*p* value < 0.001), and for every one day increase in the duration of the outbreak, the FMD total economic losses per farm increase 1.4% (*p* value $= 0.017$). The overall regression model was significant (F (2, 57) = 12.7, *p* value <0.001) with an adjusted R^2 of 0.28.

Table 3.5. Economic losses from foot and mouth disease outbreak between 2015 and 2016 in dairy cattle farms in Muak Lek district (n = 60)

Economic variables	Descriptive statistics			
	Mean	Min	Median	Max
Daily milk loss due to FMD (kg/cow/day)	5.0	0.7	4.8	17.4
Milk price (USD/kg)	0.48	0.41	0.49	0.51
Duration of outbreak (day)	21	6	28	45
Extra labour during the outbreak (hours/day)	3.5	0	4	10
Milk production loss (USD/farm)	1,063	6	726	14,688
Milk production loss (USD/animal)	19	0.1	11	128
Mortality loss (USD/farm)	532	0	0	6,286
Mortality loss (USD/animal)	18	0	0	314
Additional labour (USD/farm)	86	0	60	300
Additional labour (USD/animal)	2	0	1	19
Veterinary service and medicine (USD/farm)	661	29	600	2,514
Veterinary service and medical costs (USD/animal)	14	0.7	14	34
Total economic losses (USD/farm)	2,454	79	1,678	17,720
Total economic losses (USD/animal)	56	2	36	377

*1 USD is approximated to 35 Thai Baht according to the average exchange rate in 2016

Table 3.6 The significant variables related to the log-transformed of total economic losses per farm from foot and mouth disease in dairy farm (n=60)

Variables	coefficient	95%CI	*P* value
Intercept	5.65	4.96 – 6.35	< 0.001
Farm size	0.014	0.003- 0.026	< 0.001
Outbreak duration	0.04	0.02 – 0.07	0.017

Discussion

This study is the first to explore the epidemiological and economic impacts of FMD on farms in Thailand and is one of the few studies on the economic impact of this disease in areas where it is endemic. We found that FMD cumulative incidence and cumulative mortality on the farms varied largely between the four outbreak areas and the animal age categories. The difference in morbidity between areas might be due to differences in outbreak management between these regions. According to the Animal Epidemics Act (of Thailand) B.E. 2558, during an FMD outbreak, veterinary offices and local governments have the authority to implement movement restrictions and emergency vaccination in an outbreak zone. As a consequence, the level of outbreak response depends on the local authority's judgement, facilities, and resources in each area.

The morbidity rate in calves was significantly lower than in adult animals for both dairy cattle and beef cattle. In Thailand, it is recommended that calves receive a first vaccination dose at 4 to 6 months of age, with a booster dose one month later; however, the booster dose was frequently missed by farmers. Young animals were therefore expected to be the most vulnerable group in the population due to inadequate immunity (Sareyyüpoğlu et al., 2019), which was contradicted by our findings. This incongruity might be explained by calf management practices; most farmers keep calves in a separate housing, away from adult animals, meaning they are less likely to be in contact with other animals (Mee, 2008).

Mortality was exceedingly low in beef cattle farms, with only one dead animal reported. The low mortality on beef cattle farms might be explained by breed, as FMD clinical signs are milder in the Asian native cattle breeds commonly raised in Thailand (Kitching, 2002); only a minor percentage of beef cattle in Thailand are crossbred exotic breeds (Bunmee et al., 2018). Beef cattle in Thailand are therefore expected to be more resistant to FMD, leading to low mortality. Due to the mild clinical signs and low mortality, beef cattle farmers, especially small free-grazing beef cattle farmers, might have low incentives to vaccinate their animals, as reflected in the low vaccination percentage in beef cattle in Banpong district. The FMD vaccination campaign should be promoted among beef cattle farmers to ensure sufficient vaccination coverage.

Surprisingly, we did not find a significant association between the epidemiological impact of FMD outbreaks and vaccination practices. This finding might be explained by the poor duration of the vaccine-induced immunity. A study on antibody titres in 403 dairy cows in the Lamphaya Klang subdistrict, Thailand, showed that only 60% of the cattle had an antibody titre above the protection level three months after vaccination; moreover, this percentage decreased to 30% by five months after vaccination (unpublished data from FMD Thailand project PRP 5905021280). Another explanation might be the low specificity of the vaccine for the circulating strain. In 2016, a new FMD strain, O/ME-SA/Ind-2001d, was reported in 11 provinces of Thailand, including the provinces of our study areas (WOAH, 2017). The previous vaccine before the outbreak in 2016 might not be well compatible with the newly introduced strain. Hence it did not provide full protection.

The economic assessment of the FMD-affected dairy farms indicated that the reduced milk yield during an FMD outbreak was the most significant economic loss. However, we found a large variation in milk loss between the farms and, consequently, a large variation in the economic impact of FMD. Several factors can influence the amount of milk loss, e.g., the amount of milk production before the outbreak, the severity of the clinical signs, and the measures taken after the outbreak. We note that the milk loss in this study was calculated based on information from cows with signs of acute clinical FMD, with the implicit assumption that milk yield returned to normal after recovery; however, some studies have indicated that this might not be the case. One study in Pakistan showed that milk yields were significantly lower two months after the onset of clinical FMD (Ferrari et al., 2014b), while a study in Kenya reported an increased incidence of mastitis in the first month of the outbreak, affecting milk yields in the long term (Lyons et al., 2015). The calculation of milk loss only for cows with acute clinical signs most probably resulted in an underestimation of the actual milk loss. Moreover, more losses could occur if farmers cannot sell milk due to the outbreak control policy or market ban; for example, during the 2016 FMD outbreak in Chiang Mai province, Thailand, the milk collection centre banned milk sales from FMD-affected farms for 30 days as an FMD control measure. The average monetary losses amounted to 3,355 USD per farm (Laiya et al., 2020), which is three times higher than the milk losses without a trade ban estimated in the present study.

The second largest economic loss was mortality loss. The average mortality loss amounted to 532 USD per farm, which is half as large as the average milk loss. Because the mortality varied substantially between farms, the total losses could be very high for farms with many dead animals. The costs of additional labour, veterinary services, and other medical costs were much lower than the milk production and mortality losses. Investment in treatment and intensive management during the outbreak to reduce clinical signs and prevent mortality could therefore benefit farms. Moreover, we found that the farm size and outbreak duration were significantly related to the total economic losses per farm.

The high cumulative incidence and cumulative mortality of FMD in pig farms, especially in the Banpong district, suggests that the economic impact of FMD outbreaks in pig farms could be enormous, particularly as this disease affects pigs in all age categories (Kitching & Alexandersens, 2002). A previous study showed that the economic impact is exceptionally high in large-scale intensive pig farms (James and Rushton, 2002). Follow-up research should therefore explore the economic consequences of FMD on pig production. Moreover, pigs could be amplifier hosts that spread disease to other neighbouring farms, particularly because the amount of airborne virus dispersed by infected pigs is about 60-fold higher than ruminants (Donaldson et al., 2001). Consequently, FMD infection in pig farms could intensify the impact of outbreaks in the area, making disease control particularly important for pig farms. For beef cattle, even though FMD causes very low mortality, it could be a big hurdle when exporting beef cattle to other countries, leading to indirect economic effects. Controlling FMD in beef cattle is important to preserve the export market.

Some potential limitations of this study should be considered. First, the case definition using the clinical signs could underestimate the number of cases, especially in vaccinated animals. FMD vaccine could suppress the clinical signs and lead to subclinical infection (Kitching, 2002). Moreover, several diseases, such as swine vesicular disease, vesicular stomatitis, and bovine viral diarrhoea, show similar clinical signs as FMD, which might cause misdiagnosis (Radostits and Done, 2007). Second, we only assessed the direct economic losses. Therefore, indirect losses, such as a change in herd structure, fertility problems, and long-term effects on production (Knight-Jones & Rushton, 2013), could not be included in the economic assessment due to a lack of data. The same holds for revenues forgone, such as denied market access. As a consequence, the results of this study should be interpreted as a conservative estimation of the actual economic losses, which, in reality, may have been much higher.

This study affirms the prominence of the economic impact of FMD on dairy farms. The average yearly profit of dairy farms in Thailand amounts to 150 USD per animal (Suriya, 2015), while the average economic impact of FMD is 56 USD per animal, or one third of the annual profit. The insights of this study justify the benefit of FMD control and provide the incentive for farmers to support the FMD-control program. Moreover, Thailand is participating in a campaign to prevent, control, and eradicate FMD in South-East Asia and China (SEACFMD), and has set the goal to be FMD free with vaccination (WOAH, 2016). Perry et al. estimated the economic viability of FMD control in Thailand, revealing a benefit-cost ratio for achieving a FMD-free status of 1.72 without the potential benefits of exports (Perry et al., 1999), providing the Thai government with a high incentive for FMD control. The epidemiological and economic data from this study provide information that will help the authorities to develop and evaluate the FMD control program in Thailand.

Conclusion

This study is one of few to have reported epidemiological and economic data at the farm level in Thailand and provides insight into the factors related to the impact of FMD. It is the first study to report FMD mortality and morbidity in pig farms in Thailand. In this study, we only showed the economic impacts on dairy farms. The economic impact assessment on beef cattle and pig farms should be conducted in further study to gain insight into FMD economic loss in the endemic areas. Our results demonstrate that FMD has a prominent epidemiological and economic impact on livestock farms in Thailand, highlighting the need for, and benefit of, disease control.

Acknowledgement

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Supplementary materials

Supplementary S3.1 Epidemiological models

The model was fitted separately for each animal species. The dependent variable was the number of sick animals with clinical FMD signs in each animal category for each farm. The log number of animals at risk was used as an offset to interpret the outcome as a morbidity rate. The independent variables were the study area, animal category, and FMD vaccination practice (≤ 1, 2, and ≥ 3 vaccinations per year).

Table S3.1 The Akaike information criterion (AIC) of the models for each species. The dependent variable was the number of sick animals with clinical FMD signs in each animal category for each farm. The log number of animals at risk was used as an offset.

Species	Model	Description	AIC	df
Dairy cattle	1	Generalized Poission with intercept + areas + animal categories + vaccination	2496.0	8
	2*	Generalized Poisson with intercept + areas + animal categories	2493.3	6
	3	Generalized Poisson with intercept + areas	2528.5	4
	4	Generalized Poisson with intercept + animal categories	2530.8	4
	5	Generalized Poisson with intercept	2558.3	2
Beef cattle	1	Negative binomial with intercept + areas + animal categories + vaccination	452.8	6
	2	Negative binomial with intercept + areas + animal categories	451.7	4
	3	Negative binomial with intercept + areas	470.6	3
	4*	Negative binomial with intercept + animal categories	452.6	3
	5	Negative binomial with intercept	471.2	2
Pig	1	Negative binomial with intercept + animal categories + vaccination	627.3	6
		Negative binomial with intercept + animal categories		
	2	Negative binomial with intercept + vaccination	630.0	4
	3	Negative binomial with intercept	628.2	4
	4*		628.7	2

* the best model based on AIC. If the AIC did not differ than 2, the model with lower degree of freedom was chosen.

The dispersion parameters showed the over-dispersion of the data (the dispersion parameters in dairy cow = 4.8, beef cattle = 1.4 and pig = 55.5). Therefore, we could not use Poisson model. We fitted the generalized Poisson and negative binomial regression models with all variables. Then we tested for zero-inflation. If both models can handle zero-inflation, we choose the model that has lower AIC. After that, we used backwards stepwise based on AIC to choose the variables that were included in the final model. The AIC for each model is shown in Table S3.1.

Supplementary S3.2 Economic models in dairy farms

The linear regression models were performed to test the effect of putative risk factors on the sub-components of the total economic losses. The farm size, outbreak duration and vaccination practice were assigned as independent variables, and the natural log-transformed of milk losses, mortality losses, additional labour costs and veterinary and medicine costs per farm were assigned as the dependent variables. The results show in Table S2.2. We did not see the significant effect of vaccination practices on any sub-components of the total economic losses.

Table S3.2 The linear regression models of the log-transformed total milk losses, mortality losses, labour costs and veterinary costs per farm from foot and mouth disease on dairy farms (n=60)

Dependent variables	Independent variable	Coefficient	95%CI	*P* value
Log (total milk losses per farm)	Intercept	3.78	2.82 – 4.74	< 0.001
	Outbreak duration	0.08	0.05 – 0.11	<0.001
	Farm size	0.018	0.005 – 0.032	0.009
	Vaccination practices			
	- 1 per year	Ref.		
	- 2 per year	-0.19	-1.06 – 0.67	0.65
	- ≥ 3 per year	-0.27	-1.03 – 0.49	0.49
Log (mortality losses per farm)	Intercept	1.22	-1.57 – 4.02	0.38
	Outbreak duration	0.009	-0.078 – 0.097	0.84
	Farm size	0.006	-0.033 – 0.046	0.75
	Vaccination practices			
	- 1 per year	Ref.		
	- 2 per year	-0.29	-2.82 – 2.23	0.82
	- ≥ 3 per year	0.46	-1.76 – 2.68	0.68
Log (additional labour cost per farm)	Intercept	1.20	-0.08 – 2.49	0.07
	Outbreak duration	0.08	0.04 – 0.12	<0.001
	Farm size	0.008	-0.010 – 0.026	0.39
	Vaccination practices			
	- 1 per year	Ref.		
	- 2 per year	1.08	-0.09 – 2.24	0.07
	- ≥ 3 per year	0.21	-0.81 – 1.23	0.68
Log (veterinary service and medicine costs per farm)	Intercept	5.03	4.35 – 5.72	<0.001
	Outbreak duration	0.016	-0.005 – 0.038	0.13
	Farm size	0.02	0.01 – 0.03	<0.001
	Vaccination practices			
	- 1 per year	Ref.		
	- 2 per year	-0.37	-0.98 – 0.25	0.24
	- ≥ 3 per year	-0.25	-0.79 – 0.30	0.37


4

Chapter 4

Spatial model of foot and mouth disease outbreak in an endemic area of Thailand

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Abstract

Foot and mouth disease (FMD) is a disease of cloven-hoofed animals with high costs in animal welfare and animal production. Up to now, transmission between farms in FMD-endemic areas has been given little attention. Between-farm transmission can be quantified by distance-independent transmission parameters and a spatial transmission kernel indicating the rate of transmission of an infected farm to susceptible farms depending on the distance. The spatial transmission kernel and distance-independent transmission parameters were estimated using data from an FMD outbreak in Lamphaya Klang subdistrict in Thailand between 2016 and 2017. The spatial between-farm transmission rate in Lamphaya Klang subdistrict was higher compared with the spatial between-farm transmission rate from FMD virus (FMDV) in epidemic areas. The result can be explained by the larger size of the within-farm outbreak in the endemic area due to no culling. The inclusion of distance-independent transmission parameters improved the model fit, which suggests the presence of transmission sources from outside the area and spread within the area independent of the distance between farms. The remaining distance-dependent transmission was mainly local and could be due to over-the-fence transmission or other forms of contact between nearby farms. Farm size on the kernel positively affects the transmission rate by increasing both infectivity and susceptibility with increasing farm size. Both distance-dependent transmission and distance-independent transmission were contributed to FMDV transmission in Lamphaya Klang outbreak. These transmission parameters help to learn about FMD transmission dynamics in the endemic area.

Keywords: Spatial, Kernel, disease spread modelling, FMD, disease outbreak, farm size

Introduction

Foot and mouth disease (FMD) is an infectious disease in cloven-hoofed animals. The morbidity can reach 100% in naive populations (Davies, 2002). Foot and mouth disease virus (FMDV) infection can occur via multiple routes, including inhalation of the aerosolised virus, contact with FMDV in the environment, eating FMDV-contaminated food, direct contact with an infected animal, via skin abrasions and mucous membrane (Bravo de Rueda et al., 2015; Grubman & Baxt, 2004).

Due to high contagiousness and the wide host range, FMDV can instigate massive outbreaks, especially in FMD-free areas. During the 2001 FMD epidemic in the United Kingdom and The Netherlands, more than 6.7 million animals were slaughtered. The loss of the agricultural sector was about 3.2 billion euros, and additional costs to other sectors, such as tourism, with the sum of expenditure of about 2.7 to 3.2 billion euros (Bouma et al., 2003; Thompson et al., 2002). This outbreak triggered the inquiry into FMDV outbreak management. It is also the first time that mathematical models were introduced to manage the outbreak instead of empirical 'tried and tested' policies (Haydon et al., 2004).

The spatial features of FMDV transmission are crucial factors in its dynamics (Ostfeld et al., 2005; Wilesmith et al., 2003). Models that neglect spatial factors are oversimplified and insufficient to describe the dynamics (Riley et al., 2015). In the UK FMDV epidemic 2001, multiple studies attempted to use integrated spatial models for predicting the disease (Ferguson et al., 2001b; Keeling et al., 2001; Morris et al., 2001). Morris et al. (2001) proposed is a large complex stochastic spatial simulation model. This model is initialised with the data from the latest census, including farm size, type of livestock, and farm location in the UK. The model included a large range of transmission-related factors. Such a complex model thus required a vast number of parameters. This model was computationally intensive, and parameter estimation was limited by data availability. Moreover, the accuracy of predictions depends entirely on the validity of estimated parameters and the robustness of assumptions.

Keeling et al. (2001) proposed a simpler model that subsumed all transmission routes into a simple function called "transmission kernel". The transmission kernel is the transmission rate between farms depending on the distance between farms. The results from the model were in agreement with the spatiotemporal pattern of the 2001 UK outbreak and correctly predicted the long tail of the epidemic. Aside from distance dependence, other heterogeneous factors can also influence the kernel, for example, animal species, farm size, weather, biosecurity and management. These factors could all lead to a change in the spatiotemporal pattern of the transmission kernel and can be incorporated into the transmission kernel (Boender et al., 2014; Ster et al., 2009).

The concept of transmission kernel has been applied to FMDV models (Backer et al., 2012; Hayama et al., 2013) as well as other animal infectious disease models, e.g., risk mapping of the spread of highly pathogenic avian influenza (Bonney et al., 2018), modelling the effectiveness of vaccination strategies in classical swine fever epidemic (Backer et al., 2009), analysis of the spatiotemporal pattern of bluetongue in Western Europe (de Koeijer et al., 2011). Even though numerous FMDV models have been developed over the past years, the majority of the models were applied to epidemic areas, in particular, the United Kingdom. Only a few studies were conducted in endemic areas where most of the FMD outbreaks have happened (Pomeroy et al., 2017). Modelling FMDV outbreak in endemic areas assists local governments in designing efficient control strategies.

FMD is endemic in Thailand. Thai Government has supported routine FMD vaccination two times a year in ruminants. However, the outbreaks were reported in multiple areas of Thailand every year (Blacksell et al., 2019). In 2016, the FMD outbreaks in Lumphaya Klang subdistrict, Thailand was reported to the Department of Livestock Development. The serotyping showed that FMDV from samples belonged to serotype A. In 2017, the FMD Thailand project conducted an outbreak investigation in this area to collect additional data on farm size and the duration of an outbreak on farms.

In this paper, we used the data from the outbreak investigation to estimate the transmission kernel and the influence of farm size on the transmission kernel and introductions from outside the study area for the endemic situation from Lamphaya Klang subdistrict in Thailand between 2016 and 2017.

Materials and methods

Data collection

The study area is Lamphaya Klang subdistrict located in Saraburi province, the central region of Thailand. Saraburi province has the highest density of dairy cattle. Therefore, it is a good representation of an FMDV outbreak in a high-density cattle area. FMDV incidences were reported in dairy farms in this area between 2016 and 2017 (Figure 4.1).

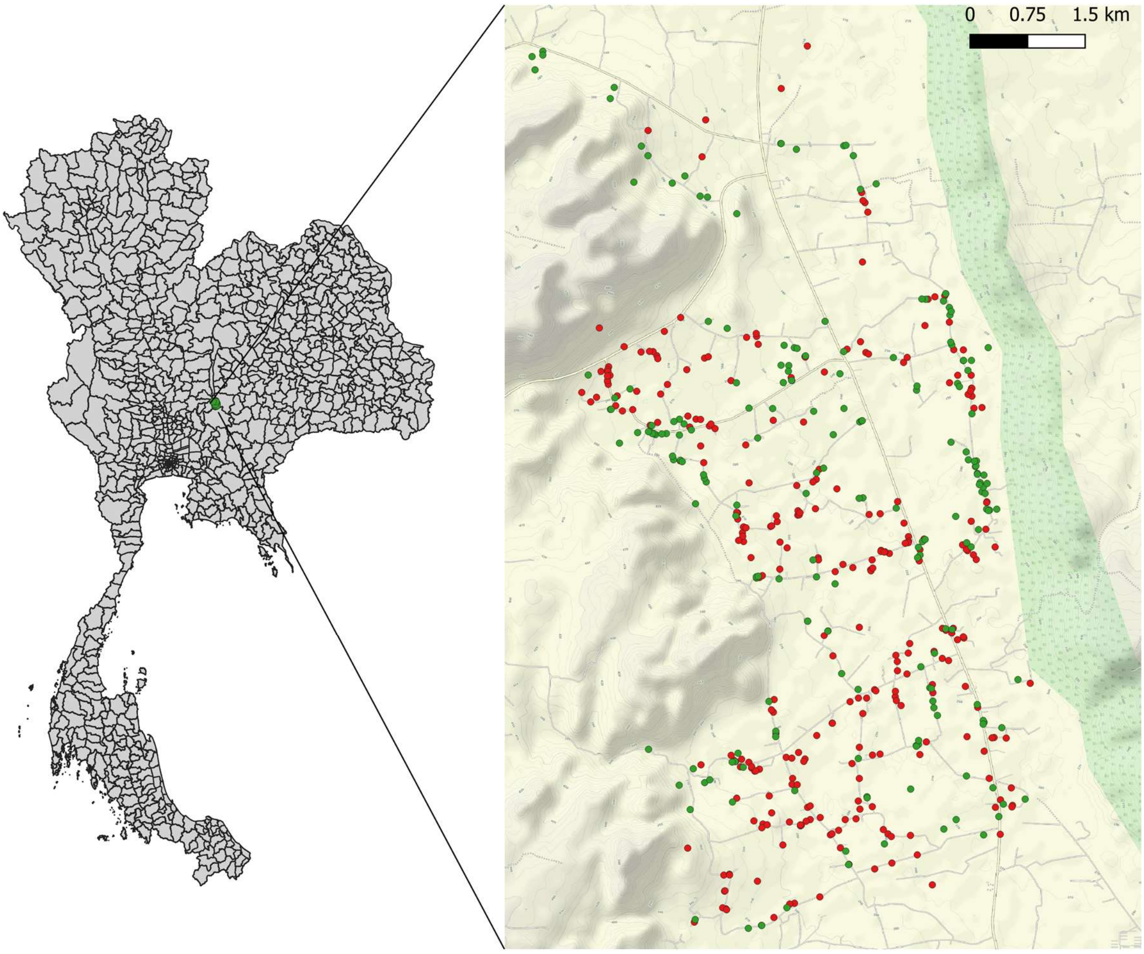

Figure 4.1 Map of the outbreak in Lamphaya Klang subdistrict in Thailand. The green dots represent the farms without FMD infection, and the red dots represent the farms with FMD infection from 15 September 2016 to 8 August 2017. The greenish area on the right side of the map represents the forest area.

We obtained the outbreak data by interviewing dairy farmers using questionnaires in the Thai language. The farm data included the geographical coordinates, the total number of animals, the number of animals with clinical signs of FMD, the date that the first animal was showing clinical signs and the date that the last animal was showing clinical signs.

The farms were selected starting at the centre of the study area at the milk collection centre in Lamphaya Klang subdistrict. We expanded the study area around the milk collection centre and collected data from every farm within the area until we reached 500 farms. This method ensured that we had data on all farms in a defined area. The study area was 12.5 by 8.4 km. In total, the dataset includes 500 dairy farms with 273 infected farms in 15 villages of Lamphaya Klang subdistrict. Other FMD-susceptible livestock species besides dairy cattle were not presented in the study area. The cases were identified by clinical signs. The numbers of the farm newly detected with FMD in each month of the outbreak from 15 September 2016 to 8 August 2017, were plotted in Figure 4.2. The total duration of the outbreak is 335 days. The average farm size in the study is 39.5, with the average infected farm size of 44.6 and the average uninfected farm size of 33.4.

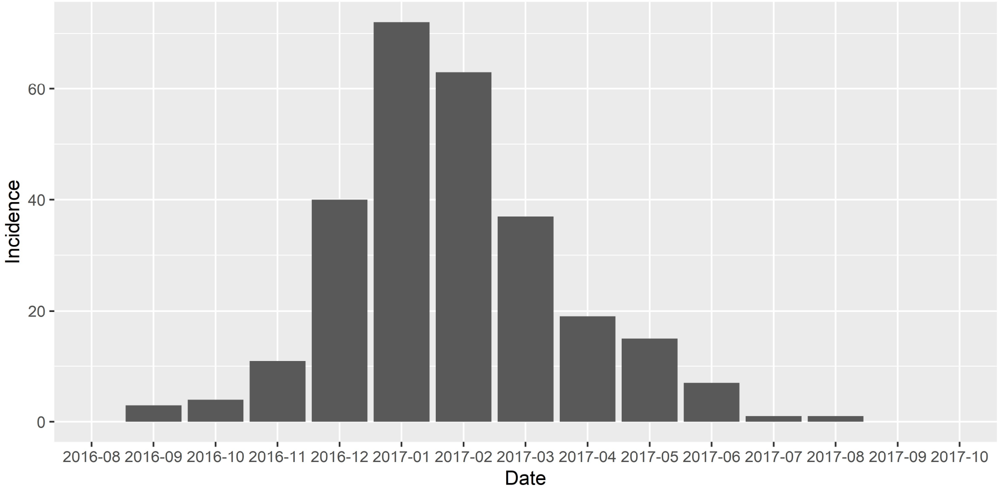

Figure 4.2 The number of newly detected FMD farms during the outbreak in Lamphaya Klang subdistrict in Thailand. The first case in this study area was reported in September 2016. The last case was reported in August 2017. In September and October 2017, no new cases were reported in this study area.

Data categorisation

The farm is the epidemiological unit in this study. Each day, the state of all farms was scored by the method described below as either susceptible, latently infected (thus not being infectious yet), asymptomatic infectious, symptomatic infectious or recovered and immunised (Figure 4.3). The infectious period, in which an infectious farm can infect another farm, is the sum of the asymptomatic infectious and symptomatic infectious period.

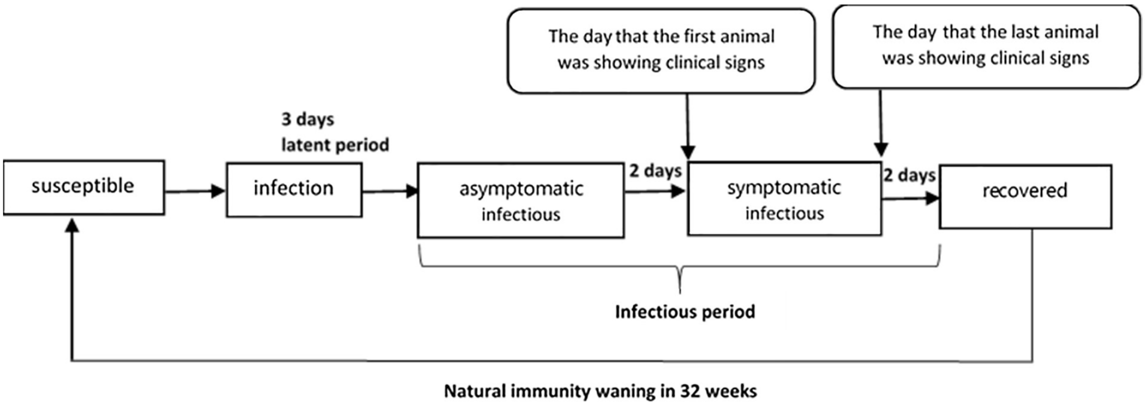

Figure 4.3 The state transition of farms during the outbreaks. The square boxes represent the state of farms being susceptible, infection, asymptomatic infectious, symptomatic infectious, recovered and immune state. The date on which each farm changes state can be estimated from the date that the first and the last animal was showing clinical signs.

All farms start having a susceptible state and become infected five days before the date that the first animal shows clinical signs. The first three days after infection are a latent period followed by two days of asymptomatic infectiousness. The symptomatic infectious period continues from the date that the first animal shows clinical signs until two days after the last animal shows clinical signs (Mardones et al., 2010). After that, farms remain in the recovered state, and we assume that the farm is immune for up to 224 days (32 weeks). The waning immunity duration is referred from the study of FMD immunity waning after natural infection in individual animals (El-Sayed et al., 2012). After 32 weeks, the natural immunity wanes and farms resume a susceptible state. The assumptions of our model are somewhat different from previous studies. In Boender et al. (2010) and Hayama et al. (2013), the farms stay infectious until the culling day. However, FMDV control strategies in Thailand do not include culling. We assume that the farm outbreaks are self-limiting due to a lack of susceptible animals at the farm. After the last symptomatic infections are recovered, these farms are protected against a new outbreak because of herd immunity within the farm.

The study period starts on the date that the first farms were infected (t_0 = 15 September 2016), which is five days before the first symptomatic farm was observed, to the date that the last farms stopped being infectious ($t_{\max}$= 8 August 2017), which was two days after the last symptoms were observed.

Transmission kernel estimation

Baseline model

We used the kernel formula presented in Eq.4.1 in the analysis. We compared this kernel formula with other formulas (Hayama et al., 2013; Ster et al., 2009). The results did not show a statistical difference between kernel formulas. Therefore, we selected this kernel formula because it was widely used in the livestock diseases studies such as FMDV, avian influenza virus, and bluetongue virus (Boender et al., 2010; de Koeijer et al., 2011; Dorigatti et al., 2010).

$$k(r_{ij}) = \frac{k_0}{1 + \left(\frac{r_{ij}}{r_0}\right)^{\alpha}} \tag{4.1}$$

The $k(r_{\mathrm{ij}})$ is the transmission rate from infectious farm j to susceptible farm i, which related to the distance between these two farms (r_{ij}).The shape of the kernel is expressed by three parameters: the k_0 parameter represents the transmission rate per day at distance zero; r_0 represents the distance for which the transmission rate is half k_0; α represents the slope at which the transmission rate decreases as a function of distance. The force of infection acting on the susceptible farm i on day t can be calculated by the sum of the kernel from all infectious farms on day t (Eq. 4.2).

$$\lambda_i(t) = \sum_{j \epsilon infectious} k(r_{ij}) \tag{4.2}$$

The distance-independent transmission

In the previous sections, the kernel was estimated under the assumption that the transmission is only caused by the infectious farms inside the study area, and the transmission rate depends on the distance between farms. Nevertheless, in an endemic situation like Thailand, there might be a possibility that the transmission originated from other sources besides the infected farms in the study area. Therefore, the h and δ parameters were introduced into the model to capture the distance-independent transmission (Eq.4.3).

$$\lambda_i(t) = \left(\sum_{j \epsilon infectious} \left(k(r_{ij}) + \delta \right) \right) + h \tag{4.3}$$

The h parameter is a constant force of infection that is independent of the number of infectious farms and the distance between farms on the susceptible farm i at day t. It can be interpreted as the force of infection from the outside area.

The δ parameter is a distance-independent transmission rate to take into account infectious farm contacts that are not determined by inter-farm distance inside the study area. The δ parameter times the number of infectious farms is a distance-independent force of infection for each of the susceptible farms.

The influence of farm size on transmission

The heterogeneity of farm size affects the transmission rate; therefore, we tested the influence of farm size on the kernel by multiplying the farm size function $(f^c(N_i, N_j))$ with the kernel in Eq.4.4.

$$\lambda_i(t) = \sum_{j \epsilon infectious} f^c(N_i, N_j) k(r_{ij}) \tag{4.4}$$

We evaluated six different farm-size functions (Boender et al., 2014)

$$f^{c}(N_i,N_j)=\begin{cases} \left(\dfrac{N_iN_j}{\bar{N}^2}\right)^{c} & for\ (1) \\ \left(\dfrac{N_i}{\bar{N}}\right)^{c_i}\left(\dfrac{N_j}{\bar{N}}\right)^{c_j} & for\ (2) \\ 1+a\left(\dfrac{N_i}{\bar{N}}-1\right)\left(\dfrac{N_j}{\bar{N}}-1\right) & for\ (3) \\ \left[1+a_i\left(\dfrac{N_i}{\bar{N}}-1\right)\right]\left[1+a_j\left(\dfrac{N_j}{\bar{N}}-1\right)\right] & for\ (4) \\ \left[1-exp\left(-\dfrac{N_i}{d\bar{N}}\right)\right]\left[1-exp\left(-\dfrac{N_j}{d\bar{N}}\right)\right] & for\ (5) \\ \left[1-exp\left(-\dfrac{N_i}{d_i\bar{N}}\right)\right]\left[1-exp\left(-\dfrac{N_j}{d_j\bar{N}}\right)\right] & for\ (6) \end{cases} \tag{4.5}$$

$f^{c}N_\mathrm{i}$ denotes the number of animals in susceptible farm i. N_j denotes the number of animals in infectious farm j. $\bar{N}$ denotes the average number of animals in all farms. The c, a and d are the farm size parameters. In (1), (3) and (5), the farm size parameters (c, a, d) are the same between infectious and susceptible farms, while in (2), (4) and (6), the farm size parameters are distinct between infectious $(c_\mathrm{j}, a_\mathrm{j}, d_\mathrm{j})$ and susceptible farms $(c_\mathrm{i}, a_\mathrm{i}, d_\mathrm{i})$.

The effect of an immune population

The baseline model assumes all farms start with a susceptible state. However, this assumption is uncertain in the FMD-endemic area. Some of the farms might have had the infection before, resulting in herd immunity. Some farms were vaccinated since routine FMD vaccination program in dairy farms is common in Thailand. The analysis was performed to determine the sensitivity of the kernel estimation to the baseline number of immune farms. We randomly assigned 25%, 50% and 75% of the susceptible farms that remained uninfected during the study period to be immune from the start of the outbreak. The model for each immune percentage was simulated 100 times to account for uncertainty. For each iteration, the transmission kernel parameters were estimated, and the kernels were calculated and plotted in Figure 4.7.

In this model, we estimated the waning immunity at 32 weeks. This assumption was referred from the experiment of natural immunity waning in individual calves (El-Sayed et al., 2012), which is almost as long as the length of the study period. Herd immunity also needs to be considered the heterogeneity among animals of immune level and population turnover. To test the uncertainty of immune waning, we analysed an additional kernel given that the recovered farms did not become susceptible again during the outbreak time frame.

Parameter estimation

The kernel parameters are estimated by maximising the likelihood function (L), which is the product of probabilities of escaping infection until the infection time of infected farms, the probabilities of escaping infection the whole study period of farms that do not become infected and the probabilities of escaping the infection after waning of immunity until the end of the study period of recovered farms (Eq. 4.6).

$$L = \prod_{m \epsilon M} \underbrace{P_{esc,m}\left(t_{inf,m-1}, t_{start}\right) P_{inf,m}\left(t_{inf,m}\right)}_{Prob.\ escaping\ until\ and\ infection\ at\ t_{inf}} \prod_{n \epsilon N} \underbrace{P_{esc,n}\left(t_{max}, t_{start}\right)}_{Prob.\ escaping\ until\ end\ of\ study\ period} \prod_{w \epsilon W} \underbrace{P_{esc,w}\left(t_{max}, t_{waning,w}\right)}_{Prob.\ escaping\ from\ waning\ until\ end\ of\ study\ period} \tag{4.6}$$

Set M contains all farms that are infected at times $t_{\text{inf,m}}$. The set N contains the susceptible farms that remain uninfected until time t_{max}. The set W contains the farms that are susceptible again after immunity waning at time $t_{\text{waning,w}}$ and these farms remain uninfected until time t_{max}. Reinfection after waning of immunity was not observed. The start of the study period is indicated by t_{start}. P_{esc} denotes the probability of the farm escaping infection until time t_{inf} , and P_{inf} denotes the probability of the farm being infected at time t_{inf}. The probability of escaping and the probability of infection follows from the force of infection Eq.4.2 assuming a Poisson process:

$$P_{esc,i}(t_{end-1}, t_0) = exp(-\sum_{t=t_0}^{t_{end,i-1}} \lambda(t)) \tag{4.7}$$

$$P_{inf}\left(t_{inf}\right) = 1 - exp(-\lambda\left(t_{inf}\right)) \tag{4.8}$$

The log-likelihood ($\ln(L)$) was used for the calculation to reduce computational complexity. The confidence interval for each parameter was obtained by the profile likelihood. The 95% confidence interval will be reported between brackets in the result. The parameter estimation and confidence interval calculation were done in R version 3.6.2 using packages "optimx" and "bbmle2". The fit of alternative models was evaluated based on the Akaike information criterion (AIC). The model with a lower AIC has a better fit, but if the AIC does not differ more than two, the models are considered to be equivalent.

Reproduction number

The reproduction number of each farm i (R_i) can be calculated by the sum of probability of infection from infected farm i to all susceptible farms j with each their own distance to farm i during infectious period T_i of that farm (Eq.4.9).

$$R_i = \sum_{j \neq i} \left(1 - E\left[e^{-k(r_{ij})T_i}\right]\right) \tag{4.9}$$

We used the actual infectious period as T_i for infectious farm i. We used a median infectious period for susceptible farms estimated from the outbreak data as T_i (15 days). If farm i has reproduction number above 1, the farm i will, on average, infect more than one other farm, thus increasing the outbreak size. As the outbreak progresses, more farms get infected, and the number of susceptible farms is depleted. To investigate whether the outbreak was limited because of the depletion of susceptible farms, we calculated the reproduction number (R_i) of remaining susceptible farms after removing the infected farms. If the R_i of remaining susceptible farms below 1, it means that the number of remaining susceptible farms is not enough for the outbreak to continue, and the outbreak is indeed limited due to the depletion of susceptible farms. We created a map of the reproduction number.

Results

Transmission kernel estimation

The transmission rate at zero distance (k_0) was estimated as 0.0054 (0.0023 - 0.012) day^{-1}, the distance where the transmission rate reached half of the maximum transmission rate (r_0) was estimated as 0.19 (0.07, 0.35) km, and the shape parameter (α) as 1.56 (1.29 - 1.84). The transmission kernel of the FMD outbreak in the endemic area of Lamphaya Klang subdistrict 2016 with independent distance parameters and function of farm size (1) was compared with the transmission kernels of FMDV outbreak in the epidemic area of the Netherlands 2001 (Boender et al., 2010) and that of the FMDV outbreak in the epidemic area of Japan 2010 (Hayama et al., 2013) (Figure 4.4).

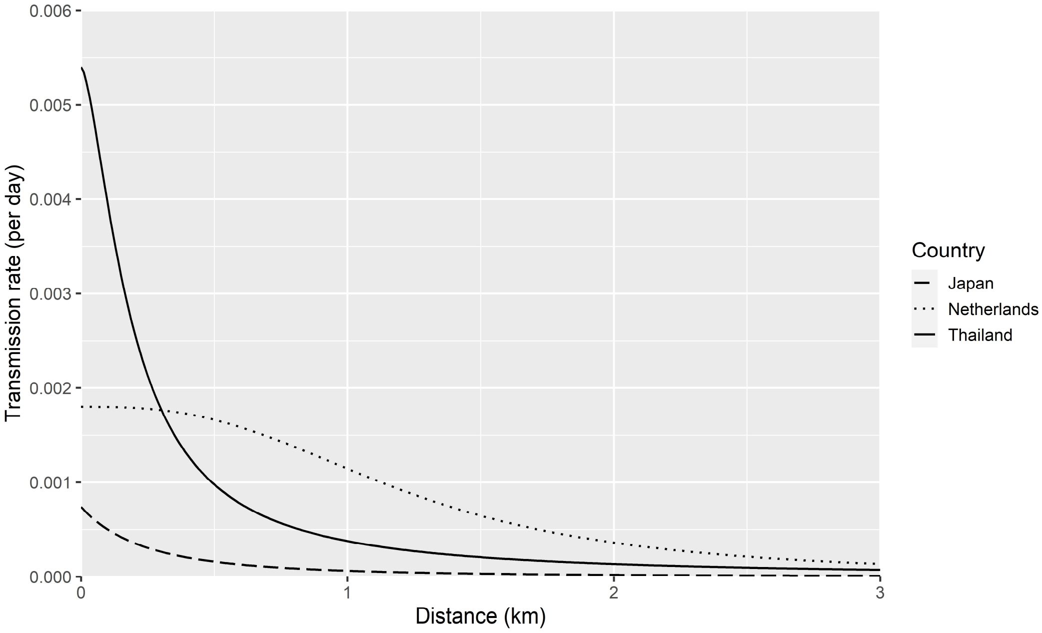

Figure 4.4 The Lamphaya Klang subdistrict 2016, Japan 2010 (Hayama et al., 2013) and the Netherlands 2001 (Boender et al., 2010) FMD transmission kernels comparison. The transmission rate (day^{-1}) experienced by one recipient farm from one infectious farm was plotted against the distance (km) between the two. The solid line represents the baseline kernel from the 2016 Lamphaya Klang subdistrict outbreak (k_0 = 0.0054 day^{-1}(0.0023 - 0.012), r_0 = 0.19 (0.07 - 0.35) km, α = 1.56 (1.29 - 1.84)). The dotted line represents the baseline kernel of the 2001 Dutch FMD outbreak (k_0 = 0.0018 (0.0004 - 0.0063) day^{-1}, r_0 = 1.22 (0.67 - 3.35) km, α = 2.8 (2.3 - 4.1)). The dashed line represents the 2010 Japan FMD outbreak (k_0 = 0.00074 day^{-1}, r_0 =0.58 km, α =2.47).

The distance-independent parameters

The inclusion of distance-independent parameters in the transmission kernel model improved the fit of the model. After including h and δ into the model, the height of the kernel reduced, and the shape became more narrow. The kernel indicated less transmission through local contacts. The parameters of the spatial transmission kernel with h and δ were k_0 = 0.003 (0.002 - 0.005), r_0 = 0.40 (0.23 - 0.63) and α = 2.80 (1.47 - 4.13) (Table 4.1, Figure 4.5).

Table 4.1 Estimated parameters, 95% profile-likelihood confidence interval and AIC for the baseline model and the models with distance-independent transmission parameters. The baseline model represents the kernel without distance-independent transmission parameters. Df denotes a degree of freedom.

Models	Optimal spatial parameter values			Distance-independent parameters	Df	AIC
	k_0 (day^{-1})	r_0 (km)	α			
Baseline model	0.005 (0.003 - 0.012)	0.19 (0.07 - 0.35)	1.56 (1.29 - 1.84)	-	3	3428.3
Model with h	0.004 (0.002 - 0.007)	0.29 (0.10 - 0.48)	1.94 (1.43 - 2.45)	$h = 2.4\times10^{-4}$ $(0.3\times10^{-4} - 4\times10^{-4})$	4	3421.8
Model with δ	0.003 (0.002 - 0.005)	0.42 (0.21 - 0.63)	2.74 (1.40 - 4.01)	$\delta = 3.6 \times10^{-5}$ $(1.4\times10^{-5} - 5.9\times10^{-5})$	4	3421.7
Model with h and δ	0.003 (0.002 - 0.005)	0.40 (0.23 - 0.63)	2.80 (1.47 - 4.13)	$h = 1.8\times10^{-4}$ $(4.1\times10^{-5} - 3.6\times10^{-4})$ $\delta = 2.6\times10^{-5}$ $(0.2\times10^{-5} - 4.9\times10^{-5})$	5	3418.6

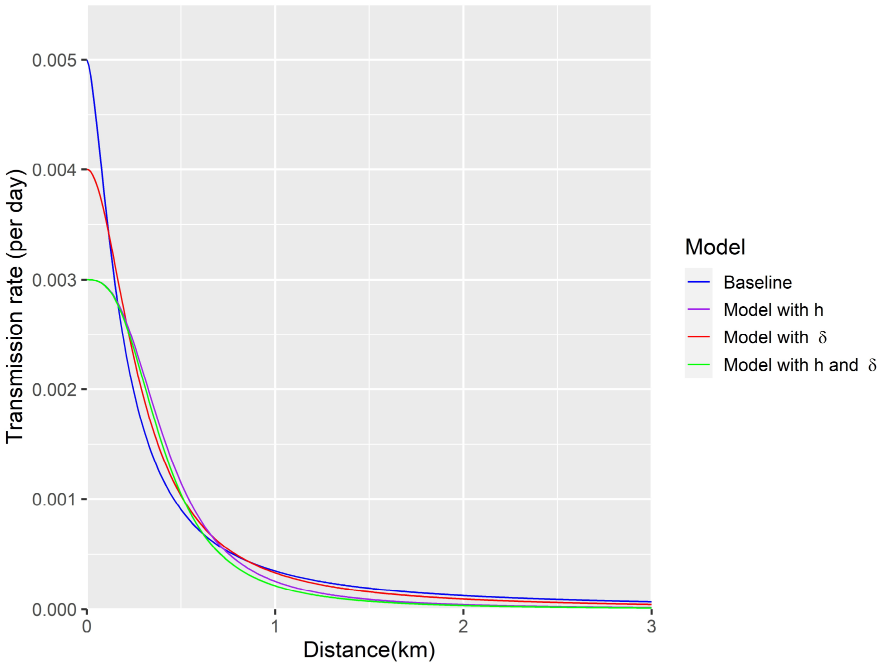

Figure 4.5 The comparison transmission kernel plot between the baseline kernel, the kernel with δ parameter, the kernel with *h* parameter and the kernel with *h* and δ parameters. The blue line represents the baseline kernel. The purple line represents the model with *h*. The red line represents the kernel with δ. The green line represents the kernel with *h* and δ.

The influence of farm size on kernel

The estimated farm size function parameters (1), (2), (3) and (4) were all positive (Table 4.2). It indicates that the between-farm transmission rate increased with farm size. In the farm size function (5), the scaling parameter of the infectious farms (d) was 0.21, which means that the infectivity rapidly increases with farm size, such that the transmission rate is 95% of the maximum transmission rate at a farm size of 25. The model for farm size function (6) did not converge. Therefore, we could not estimate the farm size function parameter.

The model with farm size function (1) has the lowest AIC. However, the difference in AIC between (1) and (2) was lower than two, which was not significant. Figure 4.6 presents the plot of the estimated transmission kernel and the prediction bounds from the baseline model and the best-fit model of farm size function (1) with different combinations of susceptible and infectious farm sizes.

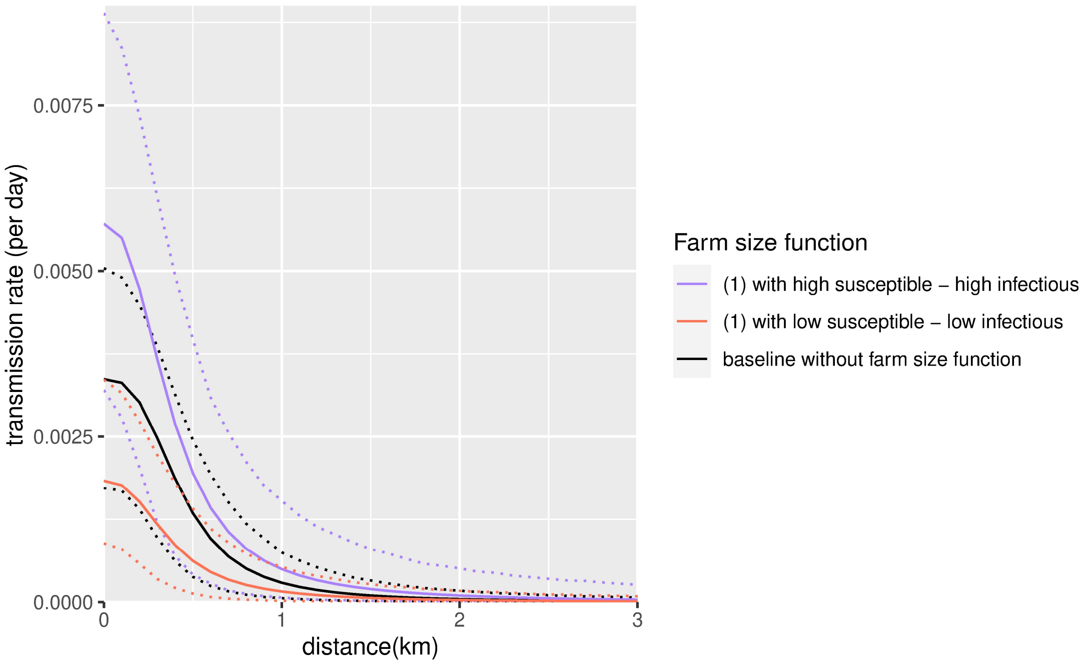

Figure 4.6 The estimated transmission kernels of the baseline model and the models with farm size function (1) in different combinations of farm size with the prediction bounds. The solid line represents the kernel from the estimated parameters. The dotted line represents the 95% prediction bounds of the kernel. The black represents the baseline kernel without the farm size function. The purple line represents farm size function (1) with a large susceptible farm size and a large infectious farm size. Large infectious farm size is the third quartile of infectious farm size $N_j = 60$. Large susceptible farm size is the third quartile of susceptible farm size $N_i = 50.5$. The orange line represents farm size function (1) with a small susceptible farm size and a small infectious farm size. Small infectious farm size is the first quartile of infectious farm size $N_j = 25$. Small susceptible farm size is the first quartile of susceptible farm size $N_i = 18$.

Table 4.2 Estimated parameters, 95% profile-likelihood confidence interval and AIC for each farm size function. The baseline model represents the kernel without farm size function, i.e., $f^c(N_i, N_j) = 1$. Df denotes the degree of freedom. The lower AIC corresponds to a better-fit model.

	Spatial parameter values					Farm size parameter values	AIC
	k_0 (day^{-1})	r_0 (km)	α	h	δ		
Base line	0.003 (0.002 - 0.005)	0.40 (0.23 - 0.63)	2.80 (1.47 - 4.13)	1.8×10^{-4} (0 - 3.6×10^{-4})	2.6×10^{-5} (0.2×10^{-5} - 4.9×10^{-5})	-	3418.6
(1)	0.004 (0.002 - 0.006)	0.38 (0.19 - 0.56)	2.44 (1.63 - 3.25)	1.7×10^{-4} (0 - 3.4×10^{-4})	2.0×10^{-5} (0.09×10^{-5}- 3.8×10^{-5})	c = 0.60 (0.40 - 0.79)	3378.8
(2)	0.004 (0.002 - 0.006)	0.37 (0.17 - 0.57)	2.40 (1.58 - 3.21)	1.7×10^{-4} (0 - 3.4×10^{-4})	1.9×10^{-5} (0.04×10^{-5} - 3.8×10^{-5})	c_i = 0.57 (0.36 - 0.79) c_j = 0.71 (0.22 - 1.20)	3380.6
(3)	0.004 (0.003 - 0.005)	0.38 (0.16 - 0.60)	2.40 (1.34 - 3.44)	1.8×10^{-4} (0 - 3.7×10^{-4})	1.9×10^{-5} (0 - 4.2×10^{-5})	a = 0.43 (-0.04 - 0.90)	3417.7
(4)	0.003 (0.002 - 0.005)	0.38 (0.18 - 0.57)	2.41 (1.60 - 3.22)	1.6×10^{-4} (0 - 3.2×10^{-4})	2.0×10^{-5} (0.1×10^{-5} - 3.9×10^{-5})	a_i = 0.64 (0.41 - 0.88) a_j = 0.69 (0.14 - 1.24)	3384.0
(5)	0.004 (0.002 - 0.006)	0.44 (0.25 - 0.63)	2.99 (1.49 - 4.48)	1.8×10^{-4} (0 - 3.6×10^{-4})	2.8×10^{-5} (0.5×10^{-5} - 5.2×10^{-5})	d = 0.21 (0 - 0.47)	3419.6

The effect of an immune population

The inclusion of a fraction of farms being immune increased the transmission rate. The transmission rate at zero distance (k_0) was higher in the model with a higher percentage of immune farms, but the distance where the transmission rate reached half of the maximum transmission rate (r_0) and the shape parameter (α) slightly changed (Figure 4.7). Assuming a longer immune period did not alter the kernel shape. The kernel of the model assumed that the recovered farms did not lose immunity until the end of the outbreak, had k_0 = 0.0059 (0.0031 - 0.013) day^{-1}; r_0 = 0.18 (0.07 - 0.35) km; α = 1.56 (1.30 - 1.87). The parameters were almost the same as the baseline model, except the k_0 was slightly higher.

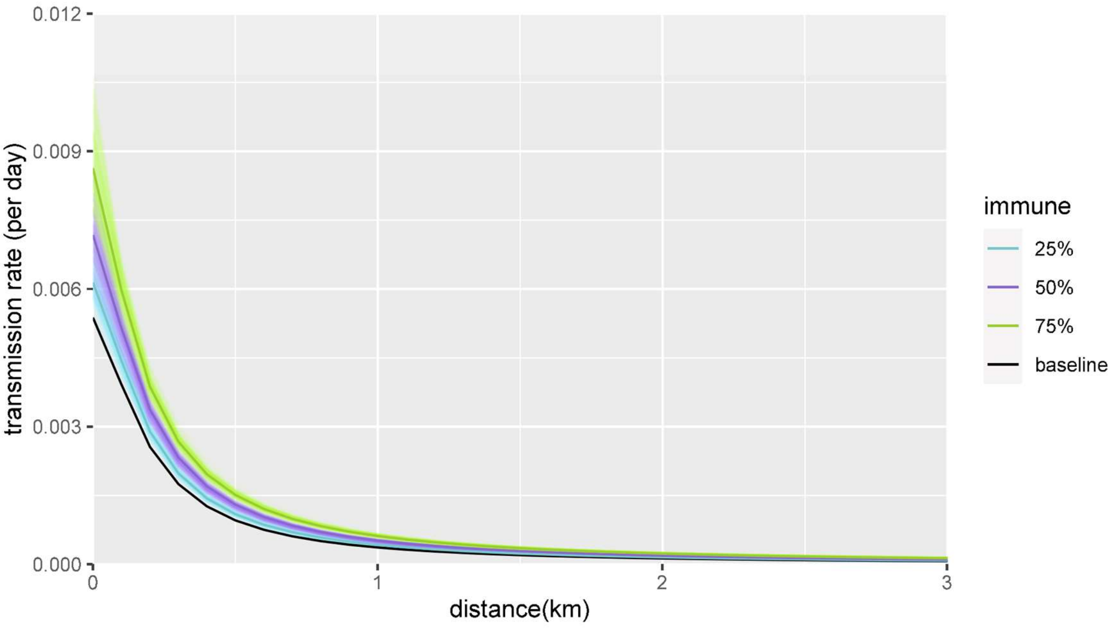

Figure 4.7 The estimated transmission kernels for each percentage of the immune farms. The blue lines, purple lines and green lines represent the kernels with the assumption that 25%, 50%, and 75% of the susceptible farms randomly became immune. The black line represents the baseline kernel.

Reproduction number

The risk map (Figure 4.8) shows farms with a reproduction number above one scattered in the centre of study areas and a number of farms with a reproduction number below 0.5 in the northern part of areas where the farms are located sparsely. After removing the infected farms, the reproduction number of the remaining farms was below one. The reproduction number of farms at the area border should be carefully interpreted since the data about farms located outside the area was unknown. Therefore, the reproduction number of farms at the area border could be underestimated.

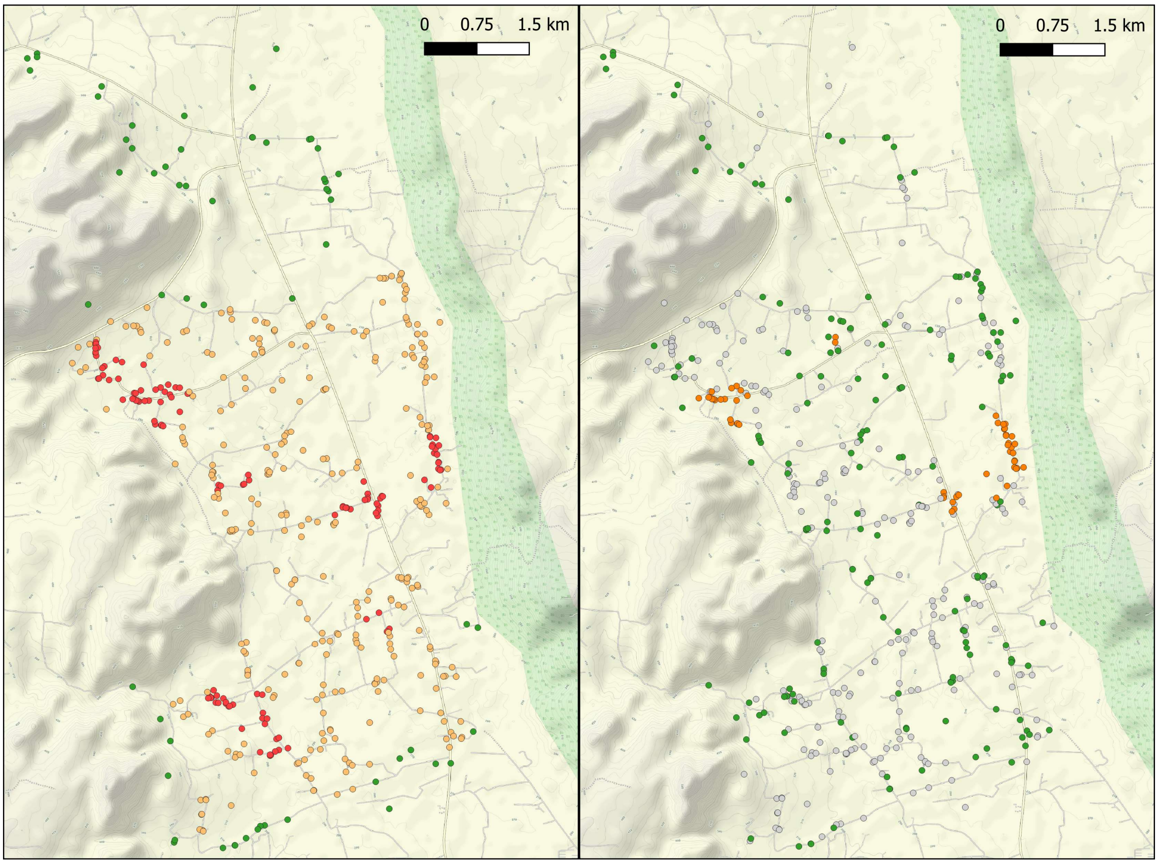

Figure 4.8 The effective reproduction number of farms was calculated using the kernel parameters with h and δ. Red dots represent the farms with $R_i \geqslant 1$; orange dots represent farms with $0.5 \leqslant R_i < 1$; green dots represent farms with $R_i < 0.5$. The left map shows the effective reproduction number considering all farms. The right map shows the effective reproduction number after removing infectious farms.

Discussion

This study is the first FMDV spatial transmission kernel estimation using the outbreak data from an endemic area. The kernel from Lamphaya Klang subdistrict shows that the transmission rate between farms drastically decreased with the distance between farms. This local transmission might be explained by a higher contact rate between nearby farms than farms that locate further. Neighbour farms might share the borders, and the risk of transmission over the fence between adjacent farms is high. Moreover, neighbour farmers are often relatives, and the contact rate between farms of relatives is likely to be relatively higher than between farms of non-relatives. Risk communication is very important to improve the awareness of farmers about FMD, so these farmers can take action to avoid local transmission. Animals should be kept away from farm borders during the outbreak to prevent over-the-fence transmission.

The between-farm transmission rate at the nearest distance (k_0) from Lamphaya Klang subdistrict was higher than the previous FMD studies from the Netherlands 2001 and Japan 2010 FMD outbreak. The higher k_0 might be explained by the size of the within-farm outbreaks in Lumphaya Klang subdistrict compared to those in the Netherlands and Japan. In the outbreak of the Netherlands in 2001 and Japan in 2010, outbreak control measures were implemented, including immediate culling of all animals at infected farms (Bouma et al., 2003; Muroga et al., 2012). Although culling might reduce the transmission rate, the adoption of a culling policy in Thailand is controversial because of the widespread occurrence of the disease. Unlike the Netherlands and Japan where regaining the FMDV-free status is the priority of control to enable the export of animals and animal products, an endemic area like Thailand might not gain full benefit from the culling because an FMDV-free status is unlikely to be obtained. Blanket vaccination of all animal in the area might be a more cost-effective intervention in the endemic area since the vaccination significantly reduces the amount of virus excretion in infected animals and also help develop immunity in susceptible animals (Barnett & Carabin, 2002). Vaccination helps to reduce the transmission rate, consequently abating the size of outbreaks with a lower economic cost than culling (Hagerman et al., 2012). According to the Animal Epidemics Act of Thailand BE 2558, the authorities can announce an outbreak zone where animal movement restrictions and emergency vaccination are implemented. However, the criteria for announcing an outbreak zone is vague and mostly depends on the discretion of the local authority. We did not find the declaration of an outbreak zone during 2016 - 2017 in our study area, so we cannot confirm the control measures during this outbreak. The outbreak was likely to be self-constrained by the depletion of the susceptible farms because the reproduction numbers of remaining farms after removing all infected farms were below one (Figure 4.8).

Some farms in the area might not have been included in the interview leading to selection bias. In case the unobserved farms also were infected, the r_0 and α from the kernel might have been biased. However, we expected that the data covered more than 95% of the farms in the area. The kernel will not noticeably change when including the unobserved farms.

From the effect of immune analysis, the transmission rate k0 between farms was higher when we initially added immune farms. The results indicated that the kernel might be underestimated if immune farms were present. Another aspect of immunity is the length of herd immunity depending on heterogeneity in individual animal immunity and population turnover. We did not observe the reinfection in the study area and period, which is in concordance with previous observations that inter epidemic period in endemic areas is about two years (Domenech et al., 2010). Therefore, we tested the robustness of kernel estimation by increasing the period of immunity. The result did not substantially change. We conclude that changing the baseline assumptions for immunity did not alter the conclusion.

The inclusion of distance-independent transmission parameters resulted in a kernel being more locally spread because the long-distance transmission is covered by the h and δ parameters. For the source of transmission from h, the study of the transmission kernel on the 2015 highly pathogenic avian influenza (HPAI) outbreak in Minnesota interpreted the h parameter as the disease introduction from wild birds (Bonney et al., 2018). It is unlikely that wildlife is the source of introduction due to the absence of cloven-hoofed wildlife in the study area, although the farmers mentioned the free-range beef cattle that sometimes enter the area. Moreover, FMDV might enter the area by vehicles, equipment and people since the movement restriction in the endemic area is lenient compared to FMD-free countries. In our analysis, we assume that h parameter is constant over the outbreak, but in reality, the probability of an incursion from outside the sub-district depends on the FMDV situation outside of the sub-district. Thus, h parameter is likely to change over time. However, we do not have information on the situation outside the outbreak to estimate the change of h parameter over time. For example, adding monthly values would increase the number of parameters and is likely to cause overfitting of the model.

The δ parameter represents the distance-independent transmission but is dependent on the number of infectious farms in the area. Though this δ parameter was small, the inclusion of δ improved the fit of the model and changed other parameter values causing a lower kernel and relatively more local transmission. One of the possible sources of δ is manure traders who buy manure from dairy farms to sell as fertiliser. They always use the same truck to pick up and deliver manure from farm to farm. Another possible source is the feed truck since many farms buy feed from the same sellers.

Including farm size statistically improved the model. The results from five different farm size functions were in agreement with each other that the susceptibility and the infectivity were increased by the higher number of animals on the infectious farms and the susceptible farms. The best-fit model was model (1), in which the relative increase in farm size results in a relatively proportional increase in the between-farms transmission rate. The susceptibility and infectivity were proportionally increased by the same exponent (c). However, the prediction bounds of the between-farms transmission rate from the model of farm size function (1) with different combinations of susceptible and infectious farm size overlap with the baseline model without farm size function (Figure 4.5.). The effect of farm size does not seem to have a relevant effect on the between-farm transmission rate. This could be due to the small variation in farm size in this area, with a minimum of 2 and a maximum of 190 (median =30). The farm size effect might be more relevant in an area with a large variation of farm size.

Our study is one of the few FMDV models in the endemic setting. Moreover, it is also the first FMDV kernel study in the endemic area. However, the kernel result should be meticulously interpreted because the heterogenous factors can affect the kernel. For example, the strain of FMDV. The 2001 Netherlands outbreak was caused by FMDV serotype O PanAsia lineage (Mason et al., 2003), and the FMDV from the 2010 Japan was caused by FMDV serotype O Mya-98 (Muroga et al., 2012), while the FMD outbreak in 2016 Lamphaya Klang subdistrict was caused by FMDV serotype A. The virulence, infectivity and transmission could be diverse between different FMD virus strains. Moreover, the species of animals also affect the transmission (Bravo de Rueda et al., 2014). The outbreaks in Japan and the Netherlands included cattle, small ruminants and pigs, but in the outbreaks in Lamphaya Klang subdistrict, only the dairy cattle farms were included in the study.

Conclusion

FMDV transmission in this outbreak consists of both distance-dependent transmission and distance-independent transmission. The distance-dependent transmission is mainly local and higher compared to the outbreak from the epidemic areas. The significant distance-independent transmission suggested that transmission from the outside and non-local transmission may happen in the outbreak. These transmission parameters help to gain knowledge about FMD transmission dynamics in the endemic area. Moreover, it could help develop a model for decision-making for outbreak response in further studies.

Acknowledgement

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Supplementary materials

Supplementary S4.1 Kernel selection

We selected the kernel formulations with varying complexity based on the previous FMD kernel. These kernel formulations will be assessed as explained by Hayama et al. (2013), and the best-fit formulation will be used for eq.1.

Kernel 1: $k(r_{ij}) = \frac{k_0}{1+\left(\frac{r_{ij}}{r_0}\right)^{\alpha}}$

Kernel 2: $k(r_{ij}) = k_0 \left(1\text{-} \exp\left(-\left(\frac{r_{ij}}{r_0}\right)^{-\alpha}\right)\right)$

Kernel 3: $k(r_{ij}) = k_0 \exp\left(-\left(\frac{r_{ij}}{r_0}\right)^{\alpha}\right)$

Kernel 4: $k(r_{ij}) = k_0 \left(1 + \frac{r_{ij}}{r_0}\right)^{-\alpha}$

The results showed that there was no difference between kernels 1, 2 and 4 (log-likelihood for kernel 1= -1711.2; kernel2 = -1711.0; kernel 3 = -1715.1; kernel 4 = -1711.9), which implied that these three formulations are not significantly better fit than others; therefore, we chose the kernel 1 for the analysis because this kernel formulation was widely used in the livestock diseases studies such as FMD, avian influenza and bluetongue.

Supplementary S4.2 Additional data and programming

The R programming code and anonymous data for models are available at: https://doi.org/10.5281/zenodo.7885504


5

Chapter 5

Evaluation of foot and mouth disease control measures: Simulating two endemic areas of Thailand

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Simulating two endemic areas of Thailand

Abstract

Foot and mouth disease (FMD) is an important livestock disease in Thailand, with outbreaks occurring every year. Despite the regular outbreaks, the study on the effect of FMD control measures is still lacking in Thailand. Epidemiological models have been widely used to evaluate FMD outbreak control. Yet, such a model has never been developed for Thailand. We constructed a stochastic between-farm transmission model to evaluate FMD control measures in two areas of Thailand, i.e. Lamphaya Klang subdistrict and Bo Phloi district, which differ amongst others in the density of the FMD-susceptible animal population. The between-farm transmission was calculated by the sum of distance-dependent transmission and trade network transmission using parameters derived from FMD outbreaks in 2016 - 2017. We used this model to simulate the outbreaks with and without the implementation of the following control measures: culling all animals on infected farms, ring vaccination, animal movement restrictions and isolation of infected farms. The control measures were evaluated by estimating the number of secondary infected farms and the outbreak duration for each scenario. The model was simulated under two study areas with high and low farm densities. The effects of control measures differed between the two study areas. In the densely populated area, rigid control measures were required to prevent a major outbreak. Among all options, culling the animals on infected farms resulted in the lowest number of infected farms and the shortest outbreak duration. In contrast, for areas with sparse farm density, less stringent control measures were enough to control the usually minor outbreaks. The results indicate that different areas require different measures to control an outbreak of FMD.

Keywords: foot and mouth disease, disease modelling, spatial transmission kernel, disease outbreak, outbreak control, control measures

Introduction

Foot and mouth disease (FMD) is considered to be the most important livestock disease in the world in terms of economic impact due to the huge economic losses from the outbreaks and their control and prevention measures (James and Rushton, 2002). For this reason, many epidemiological models have been developed to estimate the outcomes of FMD outbreaks and to evaluate different control options. This type of research has especially been carried out in FMD-free countries, for example, in the United Kingdom (Keeling et al., 2001; Morris et al., 2001), the Netherlands (Backer et al., 2012), Japan (Hayama et al., 2013) and Peru (Martínez-López et al., 2014). The simulation models developed for FMD-free countries are not suitable for applying to countries with an FMD-endemic situation because of the difference in immunity and transmission dynamics (Knight-Jones et al., 2016). Modelling FMD for an endemic situation is challenging due to the complexity of the endemic situation (Knight-Jones et al., 2016) and the scarcity of detailed data. Despite these limitations, FMD modelling for endemic areas is necessary, given the substantial impact of FMD in endemic areas (Knight-Jones & Rushton, 2013).

Over the past decades, several models have been developed to study FMD in endemic areas. For example, Lyons et al. (2021) investigated the establishment of FMD-free zones in Pakistan, Randolph et al. (2002) analysed the cost-benefit of FMD eradication in the Philippines, and similar studies were conducted on FMD control in Cambodia (Young et al., 2016) and in Ethiopia (Jemberu et al., 2016b). However, most of these studies were based on population-level incidence rather than focusing on the individual level, and the models were simplified without including the spatial element. One study in Vietnam constructed a transmission model at a commune level and incorporated spatial distance between communes (Do et al., 2022). Despite this progress, there is still a significant gap in the development of individual-based simulation models that consider spatial elements in endemic situations, especially in comparison to FMD-free countries where such models are commonly used for FMD outbreak control (Backer et al., 2012; Hayama et al., 2013; Keeling, 2005).

FMD is an endemic disease in Thailand with 980 reported outbreaks across the country from 2016 to 2021 (WOAH, 2022a). Regarding FMD outbreak control, the Thai government established an FMD outbreak control guideline in Animal Epidemics Act B.E.

2558, including multiple measures such as outbreak zone announcement, animal movement restrictions, ring vaccination and sanitary control (Arjkumpa et al., 2020b). These control measures are defined as generic regulations for every area. However, we know that FMD transmission is affected by multiple factors, such as farm density (Boender et al., 2010; Keeling et al., 2001) and animal movement (Dubé et al., 2009). As a consequence, generic FMD control measures may not be equally effective in various areas. Therefore, the objective of this research was to develop an FMD simulation model, based on the input parameters derived from the FMD outbreaks in 2016 - 2017 in two endemic areas of Thailand with different livestock species and farm densities. With this model, we could evaluate the effect of different control measures under various circumstances.

Materials and methods

Data collection

The two study areas were selected in consultation with the Department of Livestock Development. The first study area was located in Lamphaya Klang subdistrict, Saraburi province in the central region of Thailand. The area is densely populated, with a density of 7.6 farms per km^2, and 95% of farms are dairy cattle farms (Department of Livestock Development [DLD], 2019). The second study area was located in Bo Phloi district, Kanchanaburi province, in the western region of Thailand. The area consists of multiple livestock species, i.e. beef cattle, goats and pigs. This area is sparsely populated, with a density of 0.5 farms per km^2 (DLD, 2019). In these two areas, FMD outbreaks happened in 2016 - 2017. According to the official records and verification with local authorities, it was determined that no official outbreak zone was announced in both areas. Therefore, no specific control measures were implemented during the outbreaks.

The outbreak data were collected by research staff from the Faculty of Veterinary Science, Chulalongkorn University using questionnaires in October 2017 after the outbreak. The interview data consisted of the farm location, animal species, farm size, animal trading history and the history of FMD outbreaks in the farms in 2016 - 2017. The survey used a census approach The interviews started at the centre of each study area, i.e. a milk collection centre in Lamphaya Klang subdistrict and the local veterinary office in Bo Phloi district, followed by farms further away until approximately 500 farms were included. The size of the study area in Lamphaya Klang subdistrict was 12.5 × 8.4 km^2

covering 502 dairy farms. The FMD outbreak happened from 15 September 2016 to 8 August 2017 and affected 273 dairy farms. For Bo Phloi district, size of the study area was 30.8 × 25.5 km^2 covering 346 beef cattle farms, 104 goat farms and 51 pig farms, the FMD outbreak happened from 13 October 2016 to 15 December 2016 and affected 15 beef farms (Figure. 5.1). The detailed outbreak data can be found in supplementary S 5.1.

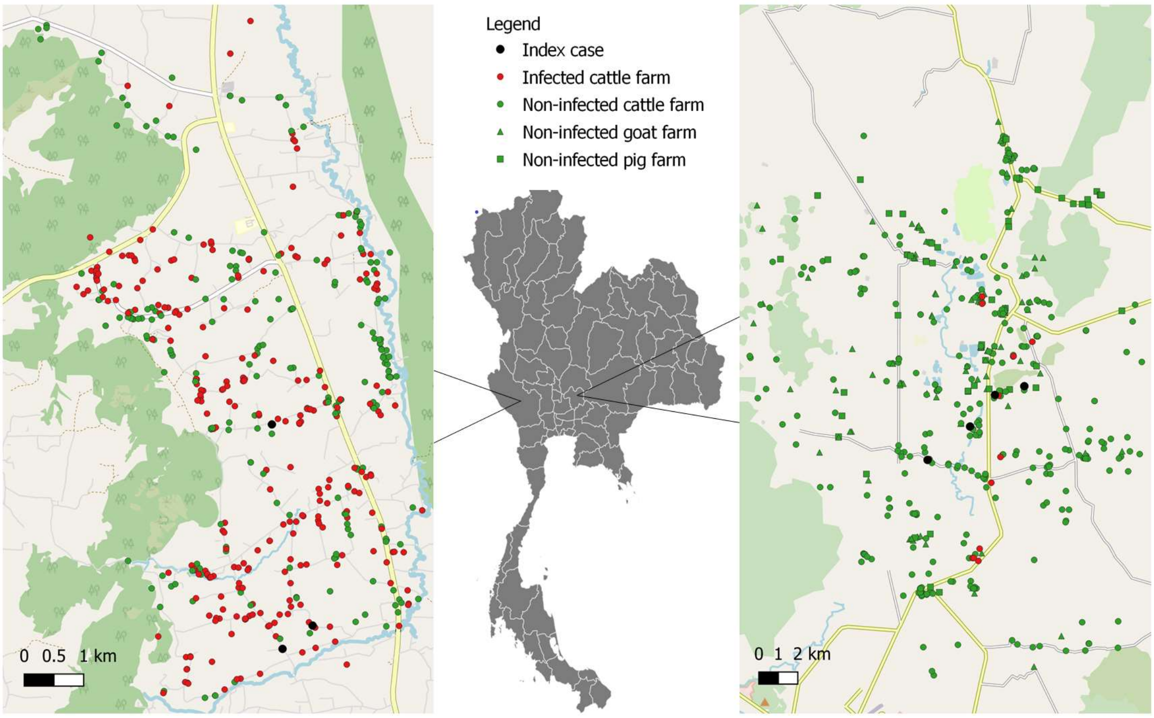

Figure 5.1 The study areas comprise of Lamphaya Klang subdistrict with an area of 12.5 × 8.4 km^2 (left) and Bo Phloi district with an area of 30.8 × 25.5 km^2 (right). It is to be noted that the scales are different between left and right maps. The circles, squares and triangles represent the cattle farms, the pig farms and the goat farms. The red colour, green colour and black colour symbolise the infected status, noninfected status and index cases in the foot and mouth disease outbreaks between 2016 and 2017, respectively.

Model outline

The model used the farm as an epidemiological unit. The characteristics of the farm, such as location, type and trade network with other farms, were based on the interview data. Each day, the model was appraised, and farm states were updated, where farms could be in the state susceptible, latent, undetected infectious, detected infectious and recovered. All farms started in the susceptible state, except for the index cases, which were in the latent state. In every simulation, we used the same set of index cases (3 farms in Lamphaya Klang subdistrict and 4 farms in Bo Phloi district based on the interview data, see Figure 5.1).

For the simulation model, the between-farms transmission was calculated via two mechanisms. The first is the spatial transmission kernel. The transmission kernel is a function describing the relation of transmission rate between the farms depending on the distance between the farms (Boender et al., 2010) (Eq. 5.1).

$$k(r_{ij}) = \frac{k_0}{1 + \left(\frac{r_{ij}}{r_0} \right)^{\alpha}} \tag{5.1}$$

Where $k(r_{\text{ij}})$ is the transmission rate exerted by infectious farm j on susceptible farm i. Parameter r_{ij} is the Euclidean distance between susceptible farm i and infectious farm j. Parameters k_0, r_0, and α determine the height and the shape of the transmission kernel. The force of infection from the transmission kernel of susceptible farm i on day t is the sum of the transmission rate from all infectious farms j to susceptible farm i on day t (Eq. 5.2).

$$\lambda_{kernel}(t) = \sum_{j \epsilon infectious} k(r_{ij}) \tag{5.2}$$

The second transmission mechanism is trade-based transmission. When the farms are infectious, they can spread the disease to other susceptible farms that share the same trader with a constant rate δ per day (Eq. 5.3).

$$\lambda_{trade}(t) = \sum_{j \epsilon infectious} \delta_{ij}\, ;\ if\ farm\ i\ sharing\ the\ same\ trader\ with\ farm\ j \tag{5.3}$$

The spatial transmission kernel and the trade transmission parameters were estimated from the combined outbreak data in the two study areas using the maximum likelihood method as previously described in Chanchaidechachai et al. (2021). The R code for the estimation of transmission parameters can be found in supplementary S5.3.

The probability of infection of a susceptible farm i on day t was calculated as the sum of the transmission kernel (Eq. 5.2) and trade transmission (Eq. 5.3) as follows:

$$p_{inf} = 1 - e^{-(\lambda_{kernel}(t)+\lambda_{trade}(t))} \tag{5.4}$$

The probability of transmission (p_{inf}) from Eq. 5.4 was used to stochastically determine the infection status. After infection, the farms were in the latent state for 3 days (Mardones et al., 2010) and then entered the undetected infectious state. The undetected infectious farms become detected infectious after a constant detection time, which was estimated from a standard SEIR model for within-farm spread. We assumed that an outbreak on a farm was detected when the number of infected animals on the farm was higher than a certain case limit depending on the livestock species (Table 5.1). During the undetected and detected infectious state, the farms were able to spread the disease to other susceptible farms. After the infectious duration, the infected farms changed to the recovered state until the end of the simulation. The model was run for 5 scenarios: (1) baseline without control measures, (2) culling all animals on infected farms, (3) ring vaccination, (4) animal movement restrictions and (5) isolation of infected farms. The details of the control measures are explained below.

Table 5.1 Summary of model parameters

Parameters	Value	Sources
Transmission kernel parameters	k_0 = 0.0054 day^{-1} r_0 = 0.171 km α = 1.50	Estimated from outbreak data using the method from (Chanchaidechachai et al., 2021)
Trade transmission rate	δ = 0.0006 day^{-1}	
Latent period	3 days	Mardones et al., 2010
Farm Infectious period in Lamphaya Klang subdistrict	Gamma (shape =3.02, rate = 0.137), mean = 22	Estimated from outbreak data
Farm Infectious period in Bo Phloi district	Gamma (shape =1.87, rate = 0.126), mean = 15	Estimated from outbreak data
Detection time for dairy cattle farm	5 days	SEIR model with the transmission rate parameter = 0.67 day^{-1} (Bravo de Rueda et al., 2015) and the number of detection cases = 2
Detection time for beef cattle farm	7 days	SEIR model with the transmission rate parameter = 0.67 day^{-1} (Bravo de Rueda et al., 2015) and the number of detection cases = 3
Detection time for pig farm	8 days	SEIR model with the transmission rate parameter = 0.59 day^{-1} (Eblé et al., 2006) and the number of detection cases = 3
Detection time for goat farm	18 days	SEIR model with the transmission rate parameter = 0.21 day^{-1} (Orsel et al., 2007) and the number of detection cases = 3

Control measures

Culling all animals on infected farms

Although culling all animals on infected farms is a common FMD control measure during FMD epidemics (European Union, 2016), culling has never been deployed to control the FMD outbreak in Thailand before. For this reason, we would like to explore the potential effect of culling in the endemic FMD situation of Thailand. For the culling scenario, we made three assumptions. First, the infected farms would be culled on a fixed number of days after detection, being 1, 7 or 14 days. Second, the culling process would be finished in 1 day, given any farm size. Third, new animals would not be reintroduced into the culled farms during the outbreak. Thus, the culled farms could not spread the disease to other farms nor be susceptible again until the end of the outbreak.

Ring vaccination

Ring vaccination is defined as the vaccination of the animals on susceptible farms in delineated areas surrounding the infected farms. We assumed that the ring vaccinations were implemented to all farms within a 10-km radius of the detected infected farms with a maximum vaccination rate of 40 farms per day and executed from outside to inside. The radius of ring vaccination was adjusted two times. The initial implementation was the area 10-km radius around the index cases. Later, the vaccination area was expanded to a radius of 10 km around the newly-detected infected farms 7 days after the detection of index cases. Vaccination induced protection against the disease after the onset of immunity. The protection from vaccines depended on vaccine efficacy, and in the model, it reduced the susceptibility of potential recipient farms and the infectivity of infectious farms. For example, suppose the vaccine efficacy was x %, then the susceptibility of vaccinated susceptible farms was 100 – x % and so on. To consider the parameter uncertainty, we tested the model with various combinations of the immunity onset (7, 14, 21 or 28 days) and vaccine efficacy (0 – 100%). Lastly, we assumed that the immunity from the vaccine lasted for 6 months.

Animal movement restrictions

Animal movement restrictions are defined as the prohibition of the movement of animals and animal products in the outbreak zone (The Royal Thai Government Gazette, 2015). We assumed that the animal movement restrictions were announced 1 day after the index cases were detected, and it was enforced until the last infected farm was recovered. It is assumed that, after the implementation of animal movement restrictions, trade transmission became zero. To the best of our knowledge, no literature has shown the effect of animal movement restrictions on the FMD transmission kernel. One study in Belgium showed that during the animal transport restrictions, the tail of the transmission kernel for a bluetongue outbreak was flattened, which implies the reduction of long-distance transmission as part of the transmission kernel (de Koeijer et al., 2011). In this model, we assumed that other transmission routes besides animal and animal product movements, such as the movement of people, vehicles and fomites and the over-the-fence transmission between the adjacent farms, are not affected by animal movement restrictions. This kind of transmission is likely to happen between farms close to each other. Therefore, we assumed that the local transmission kernel below a specific cut-off distance from the infectious farm remained the same. In contrast, above the cut-off distance from the infectious farm, the long-distance transmission kernel was assumed to be reduced, resulting from lower animal movement activities, like the effect shown in de Koeijer et al. (2011). We tested the model with various combinations of cut-off distances from 0 to 1 km and the percentage decrease of long-distance transmission kernel from 0 to 100%.

Isolation of infected farms

The costs of animal movement restrictions were enormous (Tildesley et al., 2019). In addition, the prolonged restriction can disrupt the normal flow of animals between units and lead to animal welfare problems (Knight-Jones & Rushton, 2013). Therefore, we proposed the isolation of infected farms as an alternative option. The concept is to restrict animal and animal product movements from detected infected farms exclusively. In this model, we assumed that infected farms were isolated one day after detection until they recovered. During the isolation, the trade transmission from isolated farms became zero. However, the isolation did not completely stop the spatial transmission kernel since the people and vehicles still needed to move for farm maintenance. Thus, we used the same effect as animal movement restrictions on the spatial transmission kernel of the isolated farms.

The model diagram overviewed the farm-state transition and the effect of control measures is shown in Figure 5.2.

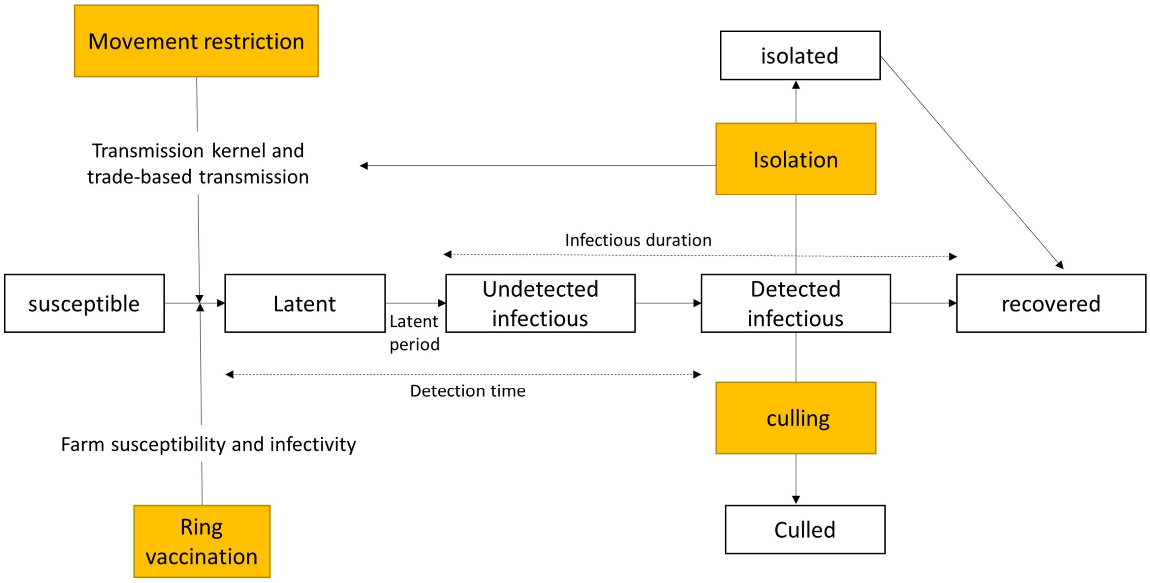

Figure 5.2 Diagram of foot and mouth disease outbreak model showing the farm-state transition (white blocks) and the effect of control measures (yellow blocks) on the parameters.

Model software and outcomes

For each scenario, the simulation started from the first day that index cases were latent to the day that the last infected farm was recovered. The simulation was run for 500 iterations to account for stochasticity. The outputs from the model were the number of secondary infected farms excluding the index cases and the outbreak duration. The model was programmed in R program version 4.2.1 (R Core Team, 2022). The R code can be found in the supplementary S5.4.

Sensitivity analysis

Global sensitivity

The global sensitivity analysis was conducted on the model parameters to assess parameter sensitivity on the number of infected farms and outbreak duration. We sampled 500 parameter sets from the parameter distribution (Table. 5.3) using Latin hypercube sampling. For each parameter set, the model was run for 100 iterations from which the predicted median number of infected farms and outbreak duration were saved. The regression-based method was used to analyse the parameters' variance contributions (Burgers et al., 2010). The regression model was fitted between the outputs and input parameters. Any type of regression model (e.g. linear regression, polynomial regression, spline regression) could be applied, but the fitted regression model needed to explain more than 90% of output variance. The sensitivity of parameters was presented by the top marginal variance (TMV) and the bottom marginal variance (BMV) which were extracted from the regression model. TMV was defined as the variance reduction that would occur if the parameter became fully known. It was calculated as the variance explained by the regression model with only that parameter. BMV was the variance that the regression model could not be explained without that parameter (Jansen et al., 1994). The sensitivity analysis was performed on 15 input parameters (Table 5.3) using the simulation outbreaks in Lamphaya Klang subdistrict. We selected the parameters with TMV of more than 25% and made scatter plots to show the effect of selected parameters on the predicted median number of infected farms and outbreak duration.

Trade network sensitivity

From the interview data, we found that approximately 20% of the farms from Lamphaya Klang subdistrict traded animals during the outbreak, but only 13% of farms could recall the traders' names, while only 6% from 12% of the farms with trading from Bo Phloi district could recall the traders' name (see the detailed trade network in supplementary S5.2). It is clear that the observed trade networks are incomplete. The real trade network between farms is expected to contain more edges than our interview data. To test the model robustness for the trade network, we simulated the trade networks assuming that 50% of the farms traded with at least one of the traders from the interview. In this simulated network, we assumed that farms could only have edges with traders, and the number of edges of each farm was randomised from the degree distribution of the trade network from interview data. The edges between farms and traders were randomly generated using the preferential attachment (Barabási & Albert, 1999). In brief, the network began with the trader nodes without any edges (degree = 0), and then the farm node was added one at a time. The edge between newly added farm node j and existing trader i was randomised with the probability equal to the number of degrees of trader i divided by the sum of all existing degrees in the network. We simulated 1,000 outbreaks with new random simulated networks in every iteration. The predicted median number of infected farms and outbreak duration were compared between the outbreaks with the simulated trade networks and the observed trade network.

Results

Baseline model

For the baseline model without control measures from Lamphaya Klang district, the predicted median number of secondary infected farms, excluding three index cases, was 293 (95% prediction interval of (0, 361)), and the predicted median outbreak duration was 312 days (95% prediction interval of (24, 469)). The number of infected farms from the real outbreak was 273 farms with an outbreak duration of 335 days. The results from the baseline model were consistent with the real outbreak data in Lamphaya Klang district. For Bo Phloi district, the predicted median number of secondary infected farms, excluding four index cases, was 3 (95% prediction interval of (0, 13)), and the predicted median outbreak duration was 42 days (95% prediction interval of (16, 116)). In comparison, the number of secondary infected farms from the real outbreak was 11, and the outbreak duration was 68 days.

Control measures

In Bo Phloi district, the effect of control measures is limited, and the differences between control measures were small due to the small baseline outbreak. In Lamphaya Klang subdistrict, all four control measures can potentially control the outbreak, but culling was the most effective in reducing the number of infected farms and the duration of the outbreak. A longer culling delay resulted in more infected farms and longer outbreak duration (Table 5.2).

The outcomes of ring vaccination were highly affected by the combination of vaccine efficacy and the onset of immunity after vaccination. The higher vaccine efficacy and the shorter onset of immunity resulted in fewer infected farms and shorter outbreak duration. The vaccine efficacy equal to or more than 60% could limit the number of secondary infected farms to less than 2, which was equivalent to the outcome of culling with a delay of 14 days (Figure. 5.3). The ring vaccination could reduce the outcomes in Bo Phloi district, as well.

Table 5.2 Predicted median and 95% prediction interval of the number of secondary infected farms (excluding index cases) and outbreak duration from the foot and mouth disease outbreak model of baseline and culling control measures in Lamphaya Klang and Bo Phloi district

Scenarios	Lamphaya Klang subdistrict		Bo Phloi district	
	Median number of secondary infected farms (95% prediction interval)	Median outbreak duration (days) (95% prediction interval)	Median number of secondary infected farms (95% prediction interval)	Median outbreak duration (days) (95% prediction interval)
Baseline	293 (1, 345)	312 (26, 506)	3 (0, 13)	42 (16, 116)
Culling with a delay of 1 day	1 (0, 7)	15 (10, 32)	1 (0, 5)	17 (14, 36)
Culling with a delay of 7 days	4 (0, 35)	34 (16, 106)	2 (0, 7)	27 (17, 54)
Culling with a delay of 14 days	21 (0, 164)	100 (23, 329)	2 (0, 11)	33 (16, 80)

Regarding the animal movement restrictions and isolation, a higher reduction of the transmission kernel and a smaller cut-off distance resulted in fewer infected farms and a shorter outbreak duration. For a transmission kernel reduction of 60% or greater, both animal movement restrictions and isolation could limit the number of secondary infected farms to fewer than 21, comparable to the outcome of culling with a delay of 14 days. If the reduction of the transmission kernel was greater than or equal to 90%, the animal movement restrictions could limit the number of secondary infected farms to fewer than 4, which was comparable to culling with a delay of 7 days (Figure. 5.3). The outbreak outcomes from animal movement restrictions were slightly lower than the isolation of the infected farms given the same parameters.

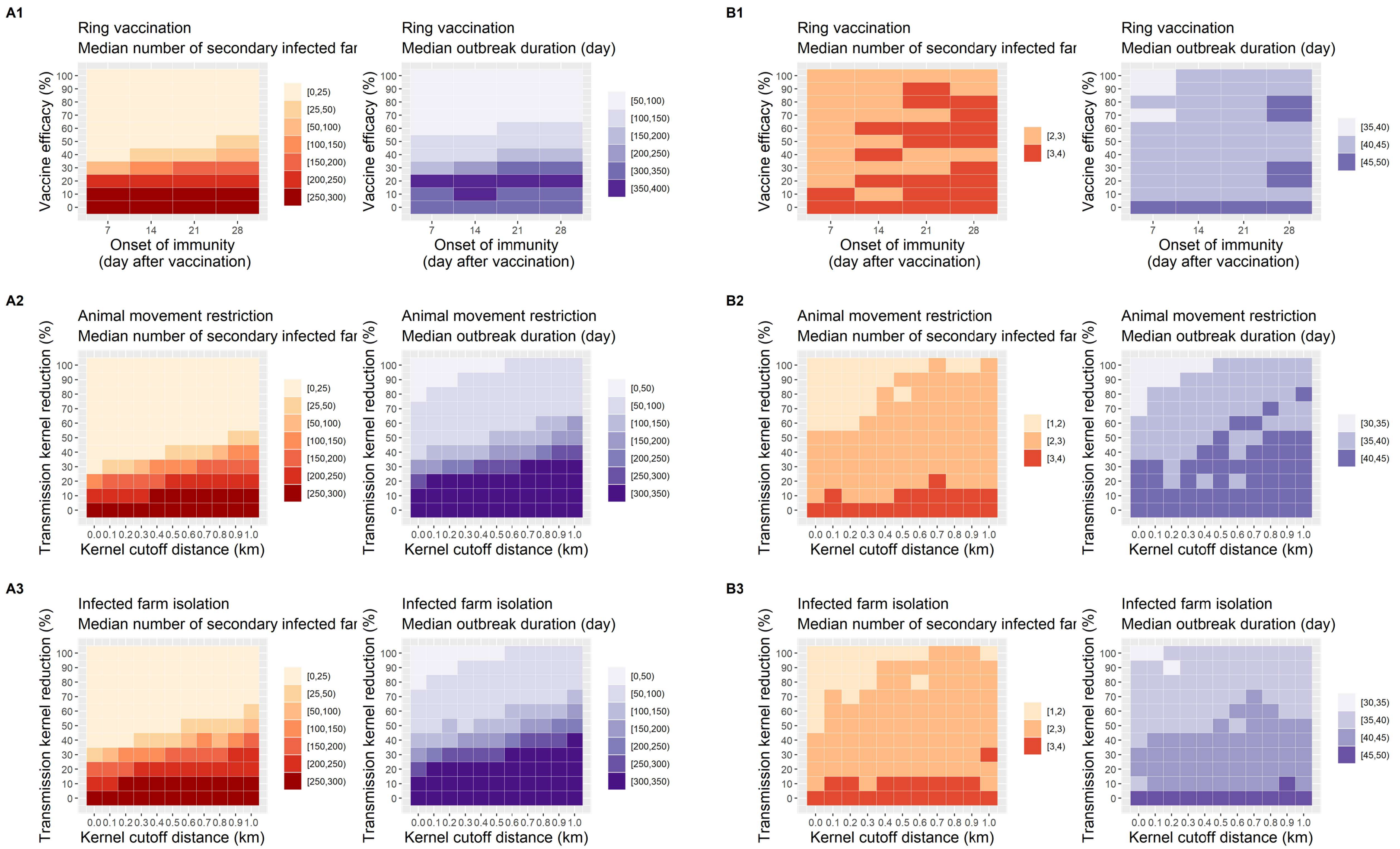

Figure 5.3 Median number of secondary infected farms (excluding index cases) and outbreak duration from the foot and mouth disease outbreak model. A1, A2 and A3 graphs represent ring vaccination, animal movement restrictions and isolation of infected farms in Lamphaya Klang subdistrict. B1, B2 and B3 graphs represent ring vaccination, animal movement restrictions and isolation of infected farms in Bo Phloi district.

Sensitivity analysis

Because the outbreak in Bo Phloi district was small, the sensitivity analysis was only performed on the models from Lamphaya Klanag subdistrict. The sensitivity analysis showed that the kernel parameters k_0 and r_0 explained most of the outcome variance in the baseline model (Table 5.3), while the transmission via the trade network (δ) barely explained the outcome variance. For the ring vaccination, outcome variance was mainly explained by the vaccine efficacy. For the animal movement restrictions and isolation of infected farms, outcome variance was mostly explained by the percentage decrease of transmission kernel.

The scatter plots in Figure 5.4 show the effect of the parameters on the simulated outcomes of FMD outbreaks. The increase of k_0 and r_0 resulted in a higher number of infected farms and outbreak duration, but at a certain point, the outbreak duration was shorter. This is caused by the high transmission rate parameter (k_0) that rapidly accelerated the transmission, which led to shorter outbreaks due to the depletion of the susceptible farms. It should be noted that the outcome variance of the isolation of infected farms was much larger than animal movement restrictions given the same parameters (Figure 5.4).

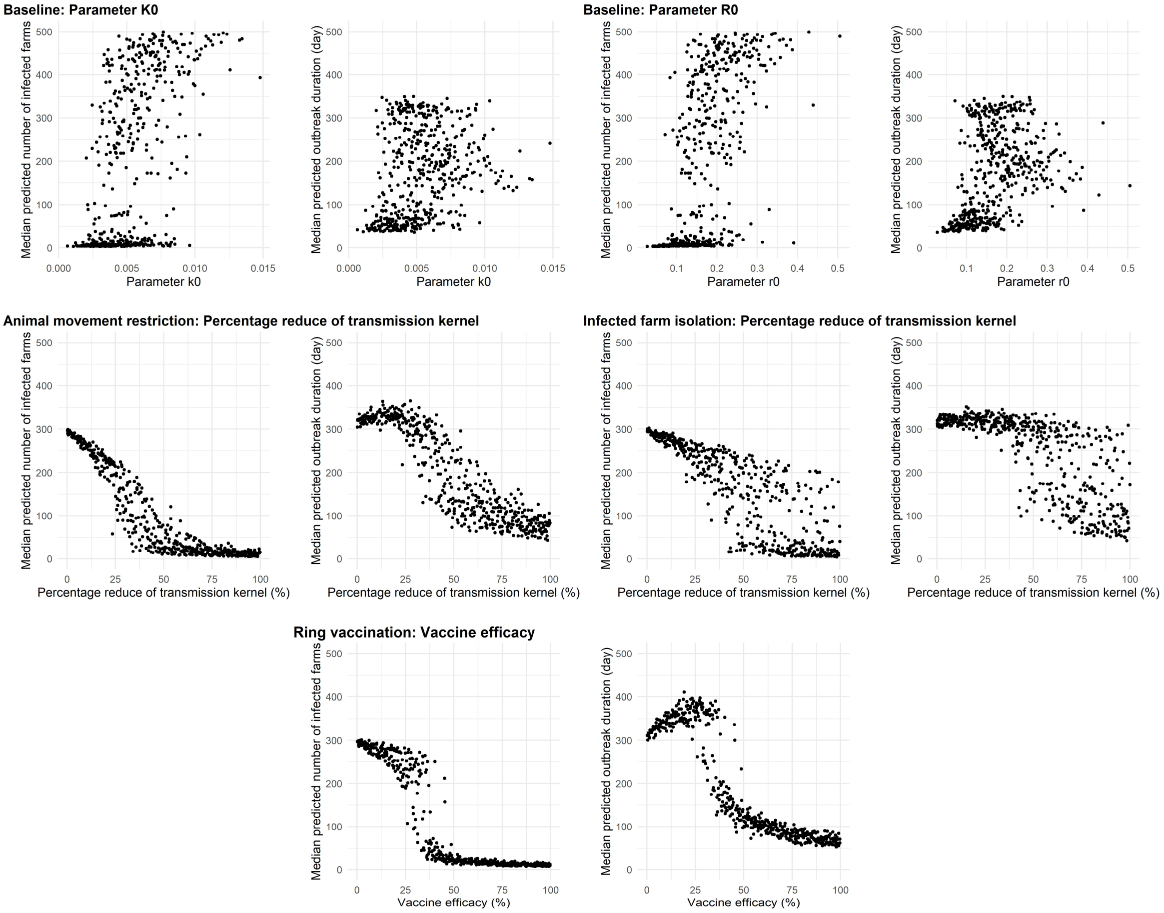

Figure 5.4 The scatter plots of the predicted median number of infected farms (left) and predicted median outbreak duration (right) against the parameters from the foot and mouth disease outbreak model in Lamphaya Klang subdistrict

From the scatter plot of ring vaccination, the low vaccine efficacy (≤ 50%) increased the duration of the outbreak compared to the zero vaccine efficacy because the low vaccine efficacy did not prevent transmission completely and did not fully protect the vaccinated farms. Thus, the virus continued to spread but at a slower pace. The ring vaccination could not stop the major outbreak until the vaccine efficacy reached approximately 50%.

Table 5. 3 Sensitivity analysis of parameters from the foot and mouth disease outbreak model in Lamphaya Klang subdistrict. Top Marginal Variance (TMV) is the variance reduction if the parameter is fully known. Bottom Marginal Variance (BMV) is the variance not explained by the parameter.

Control Measures	Parameters	Distribution	Median number of infected farms		Median outbreak duration (days)	
			Top marginal variance (%)	Bottom marginal variance (%)	Top marginal variance (%)	Bottom marginal variance (%)
Baseline	k_0	Gamma(shape = 5.25, scale =0.001)	30.7	42.7	10.4	55.6
	r_0	Gamma(shape = 5.63, scale = 0.03)	39.8	53.6	23.2	71.8
	α	Gamma(shape = 118.97 , scale =0.012)	9.6	7.8	3.1	28.6
	δ	Gamma(shape =2.18 , scale = 0.0002)	1.1	0.1	0.8	0
Ring vaccination	Vaccine efficacy (%)	Uniform(min = 0, max = 100)	86.6	87.2	93.2	90.3
	Vaccination rate (farm per day)	Uniform(min = 20, max = 80)	0	0.2	0	0.3
	onset of immunity (day after vaccination)	Uniform(min = 7, max = 28)	0	0.1	3.3	0.4
	Immunity protection duration (day)	Uniform(min = 90, max = 240)	2.1	2.1	0.9	0.4
Animal movement restrictions	Transmission kernel cut-off distance (km)	Uniform(min = 0, max = 1)	0.5	2.9	1.8	4.8
	Percentage decrease of transmission kernel (%)	Uniform(min = 0, max = 100)	91.9	94.5	81.2	85.9
	Delay animal movement restrictions (day after detection)	Uniform(min = 1, max = 30)	0.5	0.5	1.9	1.8
Isolation of infected farms	Transmission kernel cut-off distance (km)	Uniform(min = 0, max = 1)	2.6	4.1	4.1	8.9
	Percentage decrease of transmission kernel (%)	Uniform(min = 0, max = 100)	70.8	75.2	59.8	65.6
	Delay isolation (day after detection)	Uniform(min = 1, max = 14)	12.6	13.0	14.1	21.5

Trade network sensitivity

For the simulation with the increased trade network, the predicted median number of secondary infected farms was 313 (95% prediction interval of (0, 33)), and the predicted median outbreak duration was 304 days (95% prediction interval of (0, 33)) in Lamphaya Klang subdistrict. In Bo Phloi district, the predicted median number of secondary infected farms was 4 (95% prediction interval of (0, 33)), and the predicted median outbreak duration was 50 days (95% prediction interval of (16, 163)). The larger trade network resulted in a slightly larger number of infected farms and a longer outbreak duration. The distribution of outcomes from the baseline model with increased trade network simulation overlapped 99% and 94% with the distribution of outcomes from the baseline model with observed trade network in Lamphaya Klang subdistrict and Bo Phloi district, respectively (histograms in Supplementary S5.2).

Discussion

In this study, a transmission model was constructed and parameterised for two different areas of Thailand based on outbreak data. To our knowledge, this is the first FMD simulation model in Thailand that incorporated the spatial distance between farms and animal trade data. The comparison between simulation outcomes and outbreak data shows that the results from the baseline model were in accordance with the real outbreak data. Despite the slightly underestimated outbreak in Bo Phloi district, the real outbreak was in the 95% prediction interval. Thus, we argue that the observed outbreak was likely according to the model prediction, and the baseline model is valid for this area. The model could be used to assess the effect of control measures.

Based on this study's findings, culling all animals on infected farms without delay is the most effective control measure in terms of shortening the outbreak and number of infected farms. Although the culling showed a promising effect in limiting the number of infected farms and outbreak duration, the decision on culling should consider the trade-off between the cost and benefit. In an endemic country like Thailand, where the risk of outbreak recurrence is high, the cost of culling might outweigh the benefit. It is necessary to mention that this model assumed that the culling capacity is unlimited. In reality, this is not true, and with large outbreaks, culling might be delayed. Hence, the effect of culling might be overestimated in this model.

The results on ring vaccination show that given the vaccination rate and radius of ring vaccination followed the model assumption, the ring vaccination using standard vaccine with the efficacy of 75% at 4 weeks after vaccination (WOAH, 2021b) could control the outbreak. However, multiple extrinsic factors, such as vaccine matching, vaccine logistics, vaccination schedule and vaccine coverage, could lower the efficacy of vaccination in the field (Ferrari et al., 2016). In the case of outbreaks in high-risk areas or with unknown FMDV strains, we recommended using high potency FMD vaccine for ring vaccination since the high potency FMD vaccine can induce protection at 3-5 days post-vaccination and provide better protection against heterologous strains (Barnett & Carabin, 2002; Cox & Barnett, 2009).

Modelling the effect of animal movement restrictions on spatial transmission kernel is a big challenge. Since the spatial transmission kernel does not specify the transmission rate by individual transmission routes, we could not quantify how much the animal movement contributed to the transmission rate. In this study, we modelled the effect of animal movement restrictions by defining a cut-off distance from infected farms, in which the local transmission kernel below the cut-off remained the same, and the transmission kernel above the cut-off decreased faster. The cut-off distance and the kernel reduction are affected by multiple factors. The cut-off distance is affected by the farm type and management. For example, the cut-off distance from extensive farms could be higher than from intensive farms with strict biosecurity since the extensive farms are expected to have more contact with their neighbouring farms. The reduction of transmission kernel depended on the contribution of the animal movement to the overall transmission. For example, animal movement restrictions in an area with high animal movement should decrease the transmission kernel considerably and vice versa. The results were presented in various combinations of cut-off distance and transmission kernel reduction to let local authorities choose the parameters that are most likely for their area and interpret the result to reflect their situation.

In our simulation model, animal movement restrictions and isolation of infected farms both affected the transmission by reducing spatial transmission kernel and stopping the trade transmission. However, the animal movement restrictions were assumed to be applied to all detected and undetected infectious farms in the whole area. In contrast, the isolation was only applied to the isolated farms. From the median number of infected farms and outbreak duration, the isolation of infected farms was slightly inferior to animal movement restrictions (Figure. 5.3), but the variance of outcomes from isolation of infected farms was much larger than the animal movement restrictions (Figure. 5.4). This result suggests that there was a higher risk of large outbreaks in the scenario of infected farm isolation compared to the animal movement restriction scenario. It is worth noting that for the sake of simplicity, the cut-off distance and kernel reduction were the same on every farm. In reality, the effect of animal movement restrictions and isolation might be heterogenous depending on multiple underlying factors, such as farm types, biosecurity and farm contact.

Despite our best effort to collect trade network data, a part of this data could not be obtained. Hence, the partial trade network resulted in a small trade transmission parameter ($\delta = 0.0006$ day^{-1}). However, the spatial transmission kernel and trade transmission parameters were combined in the maximum likelihood estimation. The missing transmission rate from trade was captured by the spatial transmission kernel instead. The underestimated trade transmission might affect the results from control measures associated with trade, such as animal movement restrictions and isolation. These measures would have a better effect because they could completely stop trade transmission. Even with the incomplete trade network, the attempt to separate the partial trade transmission from the spatial transmission kernel was still worthwhile because this approach better depicted the real situation than using the spatial transmission kernel alone.

Overall, the results indicated that all simulated measures could control the outbreak, but the requirement for control measures to control the outbreak is different between distinct areas. For the area with high farm density, i.e. Lamphaya Klang subdistrict, the control measures needed to be more rigid to effectively control the outbreak compared to the area with low farm density, i.e. Bo Phloi district. These results suggest that the decision makers should customise the control measure based on the condition of their areas.

A few points should be noted for the model improvement in further studies. First, we assumed a homogenous baseline immunity, where all farms started with the same susceptibility level. In the endemic situation, some farms possibly have higher immunity level from vaccination and natural immunity from the previous outbreak. The heterogeneous baseline immunity might increase the spatial transmission kernel parameters, as shown by our previous study (Chanchaidechachai et al., 2021). Second, the model only focused on the transmission between the farms in the study areas without considering the risk of introducing disease to outside areas and vice versa. This risk should be included when the model is applied to a bigger scale.

Conclusion

We developed a simulation model for FMD transmission in endemic areas incorporating the spatial features and animal trade data. In the high farm density area, stringent control measures were required to prevent the major outbreak. In contrast, less stringent control measures might be chosen in areas with low farm density with usually small outbreaks, as the outbreak impact is limited. The results highlight the need for area-specific control measures.

Acknowledgements

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Supplementary materials

All code and files for project can be downloaded from https://doi.org/10.5281/zenodo.7708619

Supplementary S5.1 Outbreak data

The outbreak data were collected from 2 areas of Thailand with the FMD outbreak between 2016 and 2017. The first area is Lamphaya Klang subdistrict. The size of the study area in Lamphaya Klang subdistrict is 12.5 × 8.4 km^2 covering 502 dairy farms. The FMD outbreak happened from 15 September 2016 to 8 August 2017. The infected farms included 273 dairy farms. The second area is Bo Phloi district. the size of the study area in Bo Phloi district is 30.8 × 25.5 km^2 covering 346 beef cattle farms, 104 goat farms and 51 pig farms. The FMD outbreak happened from 13 October 2016 to 15 December 2016. The detail data The infected farms included 15 beef farms. The detail on the questionnaires and infection date estimation can be found in https://doi.org/10.1016/j.prevetmed.2021.105468. The raw data of farm type, farm size and outbreak date is available for download in the file S1.1LP_outbreak for Lamphaya Klang subdistrict and S1.2BP_outbreak for Bo Phloi district. Due to confidential data, we cannot provide the farm location. We only provided the matrix of between-farm distance (metres unit) in file for S1.3LP_distance for Lamphaya Klang subdistrict and S1.4BP_distance for Bo Phloi district.

Supplementary S5.2 Trade networks

The raw data of trade networks can be found in file S2.1Trade_network. Due to confidential data, we used ID to identify the traders. Overall, 64 farms traded and could recall the traders' names in Lamphaya Klang subdistrict. There are 48 distinct traders in the area. For Bo Phloi district, 32 farms traded and could recall the traders' names. There are 16 distinct traders.

Regarding the trade network simulation, we simulated the trade networks under the assumption that 50% of the farms traded with at least one of the traders from the interview. We assumed that farms could only have edges with traders, and the number of edges of each farm was randomised from the degree distribution of the trade network from interview data. The edges between farms and traders were randomly generated using the preferential attachment.

The histogram comparing the predicted median number of infected farms and outbreak duration between the outbreaks with the simulated trade networks and the observed trade network is shown in Figure. S5.2.1 and S5.2.2, respectively.

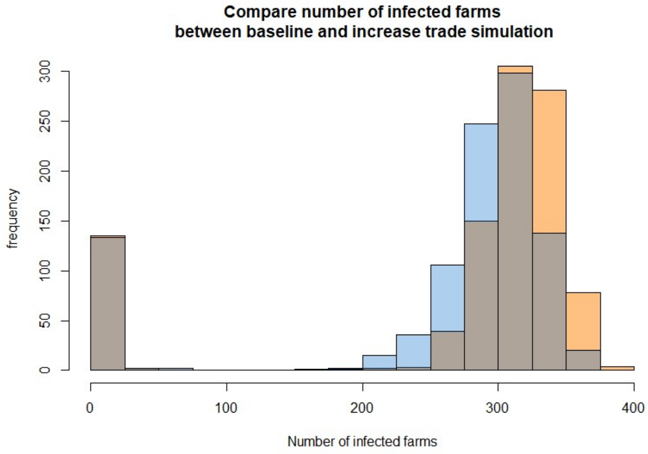

Figure S5.2.1 Histograms comparing the predicted median number of infected farms between the outbreaks with the simulated trade networks and the observed trade network. Blue histogram represents the outbreaks with the observed trade network, and orange histogram represents the outbreaks with the simulated trade networks.

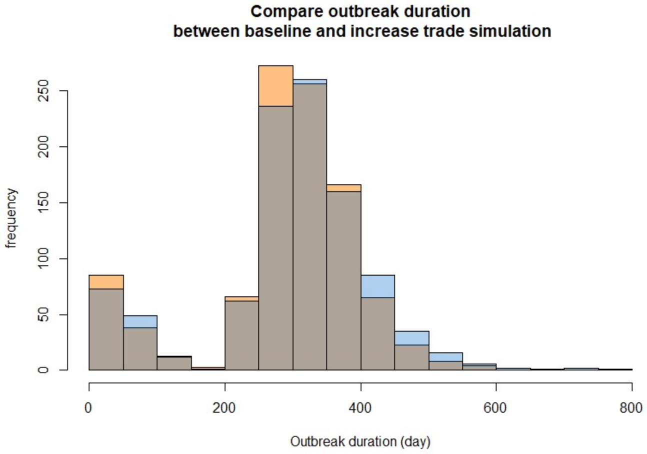

Figure S5.2.2 Histograms comparing the predicted outbreak duration between the outbreaks with the simulated trade networks and the observed trade network. Blue histogram represents the outbreaks with the observed trade network, and orange histogram represents the outbreaks with the simulated trade networks.

Supplementary S5.3 Transmission parameters estimation

The transmission parameter were estimated as the methods explained in our previous paper https://doi.org/10.1016/j.prevetmed.2021.105468. To estimate the transmission parameters, the file for outbreak data, trade network and distance between farms are required. The data from this study can be downloaded from

https://doi.org/10.5281/zenodo.7708619

Supplementary S5.4 R Model simulation

The R code for model simulation can be found in https://doi.org/10.5281/zenodo.7708619


6

Chapter 6

Cost-effectiveness of area-specific control of foot and mouth disease in Thailand

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Assessment of area-specific control of FMD

in Thailand with a bioeconomic model

Abstract

Information on the epidemiological and economic consequences of control measures is fundamental to designing effective Foot and Mouth Disease (FMD) control measures. One approach to obtaining this information is through bioeconomic modelling, which simulates outbreaks and evaluates the impact of interventions. Here, a stochastic between-farm simulation model was constructed based on data from two study areas, one high-farm-density area and one low-farm-density area, and transmission parameters derived from the FMD outbreaks in Thailand. The outputs from the outbreak simulations were the basis for an economic analysis. The results of bioeconomic model was used to assess four FMD control measures: culling of infected farms, ring vaccination, animal movement restriction and isolation of infected farms. Furthermore, the effect of farmers' compliance on cost-effectiveness of control measures was investigated. The results showed that the FMD outbreaks in the low-farm-density area were small. Hence, control measures did not significantly affect outbreak control and did not have a positive economic return. In contrast, in high-farm-density area, the FMD outbreaks were large without the control measures. Given the best parameter setting, all measures could control the outbreaks but resulted in different costs. The cost of animal movement restriction was exceptionally higher than other measures. In terms of outbreak control, culling was the best option, but it was more expensive than ring vaccination and isolation. Overall, the ring vaccination was the cheapest option given the similar outbreak control effect. If the compliance level was low, the control measures would be ineffective, resulting in high total costs of the outbreak. The cost distribution between compliant and non-compliant farms showed that the non-compliant farms paid more than the compliant farms, except for the ring vaccination, which reduced the costs for compliant farms. The results imply that the incentive for farmers to follow the measures might be small. The results highlighted the importance of area differentiation and attention to farmers' compliance when designing FMD control measures.

Keywords: foot and mouth disease, control measures, economic, disease model, bioeconomic

Introduction

Foot and mouth disease (FMD) is one of the most devastating livestock diseases in the world in terms of economic impact because of its effects on animal production and trading disruption (James & Rushton, 2002). In Thailand, FMD is endemic with outbreaks reported across the country (Punyapornwithaya et al., 2022). FMD outbreak control in Thailand has followed a general guideline. Typically, after introduction of FMD, an outbreak zone is announced, and multiple measures are implemented within the outbreak zone, including quarantine of infected premises, animal movement restrictions and ring vaccination (Arjkumpa et al., 2020b). Since the previous study showed that the size of FMD outbreaks in Thailand varies across different areas (Chanchaidechachai et al., 2022), generic FMD control measures may not be equally effective in all areas. There is a need to customise control measures based on the conditions of each area. However, the information to aid decision-makers was limited because only a few studies have been conducted on the FMD control measures in Thailand (Perry et al., 1999; Wongsathapornchai et al., 2008a; Yano et al., 2018).

Bioeconomic modelling has been commonly utilised to gain information on the effectiveness and economic feasibility of FMD control measures (Abdalla et al., 2000; Bates et al., 2003; Elbakidze et al., 2009; Jemberu et al., 2016a; Martínez-López et al., 2014). To ensure that the simulation produces sound outputs, the model must take into account the significant factors concerning disease transmission, such as farm density (Boender et al., 2010), animal species (Backer et al., 2009) and farm size (Keeling et al., 2001). Another critical factor that significantly affects the effect of control measures is the farmers' compliance (Dürr et al., 2014; Jemberu et al., 2015). Although most models have been developed under the assumption of perfect compliance, in reality, not all farmers adhere to control measures. Therefore, it is essential to incorporate the effect of compliance into the model.

In bioeconomic modelling, the epidemiological simulation outputs serve as the input for economic analysis. For the endemic situation, the economic impacts of an FMD outbreak can be estimated from direct costs from production loss and indirect costs from the implementation of control measures and revenue forgone (Knight-Jones & Rushton, 2013). Since the costs and consequences of control options vary among stakeholder groups, it is important to specify the cost distribution between stakeholders to determine the economic incentives for the stakeholder and weigh choices for a decision.

Bioeconomic modelling can provide information aiding the authority and stakeholders to design control measures. However, such an analysis has never been conducted in Thailand. Here, the bioeconomic modelling was developed by including the spatial elements of farms and parameters concerning disease transmission, i.e. farm type and farm size, to estimate the disease transmission. In addition, the farmers' compliance was included in the model to determine its effect on FMD outbreak control. The model was used to simulate the outbreak in two study areas of Thailand. We chose two study areas: Bo Phloi an area with multiple farm types at a low density and Lamphaya Klang an area with a high density of dairy cattle. The main aims of this study are to evaluate the consequences of FMD control measures in different areas and to study the effect of different measures and farmers' compliance on outbreak control.

Materials and methods

In this study we applied a simulation model for FMD outbreaks in two subdistricts with 5 intervention scenarios. The epidemiological and economic consequences of each of these scenarios were assessed. The simulation was run for 500 iterations for each scenario to account for variation. The model was programmed in R program version 4.2 (R Core Team, 2022). The R code can be found in the supplementary material S3.

Disease transmission and other parameters

The transmission between farms was calculated based on the distance from infected farms (r_{ij}), farm size (N) and farm types (cattle, goat or pig). The transmission rate $\lambda_{\mathrm{ij}}(t)$ exerted by an infectious farm j on a susceptible farm i on day t is described by:

$$\lambda_{ij}(t) = \rho_{ij} \left(\frac{N_i N_j}{\overline{N}_i \overline{N}_j}\right)^c k(r_{ij}) \tag{6.1}$$

Where ρ_{ij} is a parameter from a heterogenous transmission matrix, which was quantified from the relative infectivity of species of farm j, the relative susceptibility of species of farm i, and the assortative mixing between species (Backer et al. (2012)). The heterogeneous transmission matrix is presented in Figure 6.1.

Susceptible		Infectious		
		Cattle 1	Goats 0.5	Pig 10
	Cattle 1	1	0.5	10
	Goat 0.5	0.5	0.25	5
	Pig 0.1	0.1	0.05	1

×

Assortative mixing		
1	0.5	0.5
0.5	1	0.5
0.5	0.5	1

=

Heterogenous transmission matrix				
		Infectious		
Susceptible		Cattle	Goats	Pig
	Cattle	1	0.25	5
	Goat	025	0.25	2.5
	Pig	0.05	0.025	1

Figure 6.1 Heterogenous transmission matrix for cattle, goats and pigs calculated from the multiplication of the relative infectivity of species of farm j, the relative susceptibility of species of farm i, and the assortative mixing between species (adapted from Backer et al. (2012))

Where the farm size N_{i} denotes the number of animals in susceptible farm i. The farm sizes N_{j} denotes the number of animals in infectious farm j. $\overline{N}_{\mathrm{i}}$ denotes the average farm size for the species on farm i. $\overline{N}_{\mathrm{j}}$ denotes the average farm size of species on farm j. Parameter c is the exponent, which scales the exponential increase in the transmission rate from the increase in farm size relative to the average farm size of their own species (Boender et al., 2014).

The transmission kernel $k(r_{\mathrm{ij}})$ is a function of transmission rate depending on Euclidean distance r_{ij} between farm i and farm j, which can be explained by:

$$k(r_{ij}) = \frac{k_0}{1 + \left(\frac{r_{ij}}{r_0}\right)^{\alpha}} \tag{6.2}$$

Where r_{ij} is the Euclidean distance between susceptible farm i and infectious farm j and k_0, r_0, and α are three parameters that determine the height and the shape of the transmission kernel. The transmission parameters were estimated using a maximum likelihood method based on the outbreak data. The parameter estimation was comprehensively explained by Chanchaidechachai et al. (2021). The transmission parameters and other model parameters are presented in Table 6.1.

Table 6.1 Summary of foot and mouth disease outbreak model parameters

Parameters	Value	Reference
Transmission kernel parameters	k_0 = 0.0067 day^{-1} r_0 = 0.144 km α = 1.45	Chanchaidechachai et al. (2021)
Farm size exponent	c = 0.51	
Latent period	3 days	Mardones et al. (2010)
Farm Infectious period in Lamphaya Klang subdistrict	Gamma (shape =3.02, rate = 0.137), mean = 22	Chanchaidechachai et al. (2023)
Farm Infectious period in Bo PhloiBo Phloi district	Gamma (shape =1.87, rate = 0.126), mean = 15	
Detection time for dairy farm	5 days	
Detection time for beef farm	7 days	
Detection time for pig farm	8 days	
Detection time for goat farm	18 days	

Model outline

A stochastic between-farm transmission simulation model was applied to simulate FMD outbreaks. The farm data, i.e. farm size, farm type and location, was obtained from two study areas. The first area is Lamphaya Klang subdistrict located in the central region of Thailand, and it is highly dense with dairy cows. The second area is Bo Phloi district, which is sparsely populated with multiple livestock types, i.e. beef cattle, goats and pigs. In total, the input data included 502 dairy farms from Lamphaya Klang subdistrict, and 346 beef cattle farms, 104 goat farms and 51 pig farms in Bo Phloi district (Chanchaidechachai et al., 2023). The model was constructed with the farm as an individual unit and daily time step. The farms could be in one of the following states: susceptible, latent, undetected infectious, detected infectious or recovered. Each simulation started with three, randomly selected, infectious farms and continued until there were no infectious farms in the area. The between-farm transmission, explained in Eq.6.1, was used to calculate the probability of infection p_{inf} in Eq.6.3.

$$p_{inf} = 1 - e^{-\lambda_{ij}(t)} \tag{6.3}$$

The newly infected farms remained latent for three days before transitioning to the undetected infectious state and later transitioning to the detected infectious after detection time (Table 6.1). After the infectious duration, the infected farms became recovered and remained in this state until the end of the simulation.

Control measures

The model was used to simulate the outbreaks under five scenarios, including (1) baseline without control measures, (2) culling all animals in the infected farms, (3) ring vaccination, (4) animal movement restrictions and (5) infected farms isolation. The parameters for each control measure are summarised in Table 6.2.

The assumptions and parameters for each control measure are explained below.

Culling all animals in infected farms

All animals in infected farms were culled after 1, 7 or 14 days after the disease detection in the farms and immediate. The culling capacity was unlimited. Disease transmission stopped immediately at culling, and new animals were not reintroduced into the culled farms until the end of the outbreak.

Ring vaccination

The ring vaccination started one day after the detection of the first index case and executed from outside-to-inside within a 5-km radius of the detected infectious farms with a maximum vaccination rate of 40 farms per day. The radius of the ring vaccination was adjusted twice: initially, it was set at 5-km around the index farms, and secondly, it was expanded to 5-km around newly detected infected farms seven days after the detection of index cases. The protection started 14 days after vaccination and lasted for 6 months. The vaccine efficacy was set to 25%, 50%, 75% or 100%. The vaccine efficacy determined the susceptibility of recipient farms and the infectivity of infectious farms. For example, suppose the vaccine efficacy was *x* %, then the infectivity of vaccinated infectious farms was 100 – *x* % and so on.

Animal movement restrictions

The animal movement restrictions were enforced 7 days after the detection of the first infected farm. In the simulations, movement restriction was assumed only to affect transmission at distances above a specific cut-off distance from the infectious farm. Assuming that movement restrictions would not impact short-distance transmission through routes such as aerosols, visitors, or transmission over fences, the transmission remained the same below this cut-off distance. Long-distance transmission above the cut-off distance from the infectious farm was assumed to be reduced by a certain percentage. The cut-off distances at 0 and 1 km and the percentage decrease of long-distance transmission kernel at 25%, 50%, 75% and 100% were tested.

Isolation of infected farms

The infected farms were isolated a day after detection until the farms were recovered. During the isolation period, the farms were prohibited from moving animals and animal products. The effect of isolation on transmission parameters was assumed to be the same as animal movement restrictions but only applied to isolated farms.

Table 6.2 Summary of parameters concerning foot and mouth disease control measures

Control measures	Parameters	Values	Unit
1. Culling infected farms	Delayed culling	1,7, 14	Days after disease detection on the farms
2. Ring vaccination	Vaccine efficacy	25, 50, 75, 100	% protection
3. Animal movement restrictions	Cut-off distance	1, 0	Km
	Transmission kernel reduction	25, 50, 75, 100	% kernel reduction
4. Isolation of infected farms	Cut-off distance	1, 0	Km
	Transmission kernel reduction	25, 50, 75, 100	% kernel reduction

The effect of farmers' compliance

The farmers' compliance was modelled by randomly selecting a certain percentage of farmers to be the compliers who followed the control measures during the outbreak, and the rest of the farms were non-compliers who did not follow the control measures. For example, in the culling scenario, the non-compliant farms will not be culled despite being infected, and vice versa. The compliance level of 25%, 50%, 75% and 100% were set in the model.

Economic analysis

The outputs from outbreak simulation, e.g. number and type of infected farms, number and type of farms affected by control measures, duration of the outbreak within the farm, and duration of animal movement restrictions and isolation, were subsequently used to calculate economic impacts. In this study, the costs of FMD consisted of the direct costs from disease, including the production losses, dead animals and treatment, and the indirect costs from the implementation of control measures. The costs were specified for the two main stakeholder groups, i.e. farmers and the government (Table 6.3), and separately calculated for complying and non-complying farmers. The number of sick and dead animals in the infected farms was calculated proportionally to the mortality and morbidity rate retrieved from the literature (Table 6.4) and farm size from interview data (Chanchaidechachai et al., 2023).

Table 6.3 The costs concerning foot and mouth disease specified by control measures and stakeholder groups

Costs	Control measures					Stakeholder groups
	Baseline (no control measures)	Culling infected farms	Ring vaccina tion	Animal movement restriction	Infected farms isolation	
1. Production loss	×		×	×	×	Farmers (complying and non-complying)
2. Culling operation		×				Government
3. Idle production after culling		×				Farmers (complying)
4. Diagnostic test		×			×	Government
5. Farm disinfection and cleaning		×			×	Government
6. Vaccine and administration			×			Government
7. Production on hold				×	×	Farmers (complying)
8. Animal movement restriction operation				×		Government
9. Isolation of infected farms operation					×	Government

Table 6.4 Morbidity and mortality rate from foot and mouth disease by animal species

Animal species	Animal categories	Morbidity (%)	Mortality (%)	Reference
1. Dairy cattle	Calf	15.8	1.2	Chanchaidechachai et al. (2022)
	Heifer	28.8	0.1	
	Lactating cow	41.3	0.5	
	Dry cow	15.9	0.3	
2. Beef cattle	Young	9.1	1	
	Adult	41.5	0	
3. Pigs	Young (suckling and weaner)	17.6	8.5	
	Sow	32.5	3.4	
	Fattener	18.4	0.7	
4. Goats	Young	15	10	Senturk & Yalcin, (2012)
	Adult	15	2	

Production losses were the sum of mortality loss, treatment cost and milk production loss in dairy farms or reduced growth in beef cattle, goat and pig farms. The milk production losses were calculated based on the amount of milk reduction during FMD illness without considering the long-term effect on milk production after recovery (Chanchaidechachai et al., 2022). The reduced growth was calculated based on the additional feed cost required to fatten sick animals during the delayed days to target weight. The delayed days were assumed to be equal to the duration of the illness and to had no compensation growth after recovery. The mortality loss was calculated based on the market value of live animals. The treatment cost was a sum of medicine costs for sick animals. The parameters concerning production losses can be found in Table 6.5 a, and the detailed economic calculation can be found in Supplementary S6.2.

Regarding the organisation costs for culling, the government was responsible for covering the costs of culling operation, including diagnostic tests before culling, culling, logistics, carcass disposal, disinfection and compensation. After the culling, the culled farms were left idle for the remainder of the outbreak, in which farmers paid the fixed cost to maintain the farms. Regarding the costs for ring vaccination, the government was responsible for covering the entire cost of a ring vaccination operation, including the cost of the vaccine and any associated logistics and administration costs.

Table 6.5a The costs associated with foot and mouth disease control measures and production losses

Cost	Description	Value	Unit [a]	Stakeholders
1. Production loss	1.1 Milk production loss	2.87	€/animal/ day	Dairy farmers
	1.2 Reduced growth loss			Beef cattle, goat and pig farmers,
	Young cattle (0-12 months)	0.48	€/animal/ day	
	Adult cattle	1.69	€/animal/ day	
	Young pig (suckling and weaner pigs)	0.45	€/animal/ day	
	Adult pig	0.94	€/animal/ day	
	Young goat (0-6 months)	0.11	€/animal/ day	
	Adult goat	0.22	€/animal/ day	
	1.2 Mortality loss			Farmers
	Young cattle (0-12 months)	84.03	€/animal	
	Adult cattle	1120.45	€/animal	
	Young pig (suckling and weaner pigs)	70.03	€/animal	
	Adult pig	190.48	€/animal	
	Young goat (0-6 months)	28.01	€/animal	
	Adult goat	92.44	€/animal	
	1.3 Treatment cost			Farmers
	Young cattle (0-12 months)	14.01	€/animal	
	Adult cattle	25.21	€/animal	
	Young pig (suckling and weaner pigs)	0.42	€/animal	
	Adult pig	2.8	€/animal	
	Young goat (0-6 months)	0.42	€/animal	
	Adult goat	0.84	€/animal	

[a] Prices were originally collected in Thai baht (Thai currency) and converted into euro using the study period's average exchange rate of 35.7 Thai baht/euro

Regarding the Organisation costs for animal movement restrictions, the costs concerning the movement restriction zone execution, i.e. checkpoint setting, disinfection and labour, were paid by the government. Following the implementation of animal movement restrictions, farms were prohibited from selling their animals or animal products. The effects varied on different types of farms. The dairy farms were unable to sell their milk and forced to discard milk without any return. Animal movement restrictions affected pig farms by prolonging the time that animals need to stay on the farms leading to increased costs in two ways: (i) for fattening pigs, the price per kilogram of meat declined due to the lower percentage of red meat after reaching the finishing weight of 120kg, and (ii) for weaning pigs, the cost of feed increased during the extended period. The housing capacity of the farms was assumed to be unlimited. In the case of beef cattle and goat farms, there was no weight limit for slaughtering. Therefore, farmers could continue to fatten their animals during animal movement restrictions and potentially increased profits. As a result, there was no cost associated with animal movement restrictions for the beef cattle and goat farms.

The government was responsible for the organisation costs associated with isolating infected farms, including monitoring the isolated farms, conducting disinfection, and performing diagnostic tests before releasing the farm from isolation. The costs for farmers were the same as those associated with animal movement restrictions, but they were only applied to the isolated farms. The parameters for the economic calculation concerning control measures are shown in Table 6.5b. The detailed economic calculation can be found in Supplementary S6.2.

Table 6.5b The costs associated with foot and mouth disease control measures and production losses

Cost	Description	Value	Unit [a]	Stakeholders
2. Culling operation	2.1 Euthanasia, , carcass disposal and compensation			Government
	Young cattle (0-12 months)	93.87	€/animal	
	Adult cattle	1150.11	€/animal	
	Young pig (suckling and weaner	71.46	€/animal	
	pigs)	200.31	€/animal	
	Adult pig	29.44	€/animal	
	Young goat (0-6 months)	95.41	€/animal	
	Adult goat			
3. Farm disinfection and cleaning	3.1 Costs for farm disinfection and cleaning			Government
	Cattle small size (n <= 20)	5.6	€/farm	
	Cattle medium size (n = 21 -100)	14.01	€/farm	
	Cattle large size (n >100)	28.01	€/farm	
	Pig small size (n = 50-500)	5.6	€/farm	
	Pig medium size (n = 500 -5000)	28.01	€/farm	
	Pig large size (n > 5000)	56.02	€/farm	
	Goat small size (n <=20)	5.6	€/farm	
	Goat medium size (n = 21-100)	11.2	€/farm	
	Goat large size (n >100)	16.81	€/farm	
4. Diagnostic test	4.1 Cost for diagnostic test before culling	100.84	€/farm	Government
5. Idle production after culling	5.1 Idle production cost			Farmers
	Dairy cattle farms	1.1	€/animal/ day	
	Beef cattle farms	0.28	€/animal/ day	
	Pig farms	0.02	€/animal/ day	
	Goat farms	0.03	€/animal/ day	
6. Vaccine and administration	6.1 Vaccination			
	Young cattle (0-12 months)	1.85	€/animal	
	Adult cattle	2.71	€/animal	
	Young pig (suckling and weaner	1.06	€/animal	
	pigs)	1.71	€/animal	
	Adult pig	1.2	€/animal	
	Young goat (0-6 months)	1.48	€/animal	
	Adult goat			
7. Production on hold	7.1 Milk trade ban cost	8.15	€/animal/ day	Dairy farmers
	7.2 Lower meat price loss	0.03	€/ kg body weight	Pig farmers (fattening pigs)
	7.3 Costs for additional feed for young pig during the prolonged period	0.45	€/animal/ day	Pig farmers (Weaner pigs)
8. Animal movement restriction operation	8.1. Machine and barriers	425.77	€/ checkpoint	Government
	8.2 Labour and fuel	537.82	€/checkpoint/ day	
9. Isolation of infected farms operation	9.1 Isolated farm monitoring	3.36	€/ farm/ day	Government

[a] Prices were originally collected in Thai baht (Thai currency) and converted into euro using the study period's average exchange rate of 35.7 Thai baht/euro

Results

Outbreak control in the low-farm-density and high-farm-density area

The predicted number of infected farms, outbreak duration and total outbreak costs from the baseline scenario and the control measures with the best parameter setting, i.e. culling infected farms with the delay of 1 day, ring vaccination with 100% vaccine efficacy, animal movement restrictions and isolation infected farms that could reduce 75% of the kernel transmission and 0 km cut-off distance, are compared for the two study areas in Figure 6.2.

In the low-farm-density area of Bo Phloi district, the outbreaks were small even without control measures. In the baseline scenario, the predicted median number of infected farms was 3 (95% percentile of 13), and the predicted median total cost was 0.9 thousand euros (95% percentile of 108.8 thousand euros). The control measures had a small impact on reducing the number of infected farms and resulted in higher total costs compared to the baseline. In contrast, the outbreaks in Lamphaya Klang subdistrict, which was a high-farm-density area, were large without control measures. The predicted median number of infected farms was 272 (95% percentile of 310). The median total cost for the baseline situation was 231.6 thousand euros (95% percentile of 261 thousand euros). All control measures could limit the outbreak and reduce the total cost from the baseline, except animal movement restrictions, in which the total costs were exceptionally higher than the baseline (median total cost of 4.08 million euros). Due to the small outbreak in Bo Phloi district, the effect of control measures was small and not cost effective . Therefore, only the results from Lamphaya Klang subdistrict were presented in the following section. Additionally, we have excluded the results from animal movement restrictions from the following section, as this measure incurred exceptionally high costs and is not a sensible option to consider. However, the results from Bo Phloi district and animal movement restrictions are available in Supplementary S6.1.

The effect of control measures in Lamphaya Klang

The comparison of control measures with different parameters in Lamphaya Klang subdistrict is presented in Table 6.6 Based on the finding, culling all animals in the infected farms was the most effective measure to limit the number of infected farms and the duration of an outbreak. Culling with a delay of 1 day reduced the predicted median number of infected farms to 1 (95% percentile of 4). The outcomes of culling became worse when the number of delayed days before culling increased. Still, at 14 delayed days, culling could limit the number of infected farms. Regarding the costs, culling was more expensive than ring vaccination and isolation of infected farms, which gave similar epidemiological outcomes. Most culling costs were incurred through the indirect costs related to the culling operation. With a delay in culling, the indirect costs increased.

In terms of outbreak control, the effect of ring vaccination and isolation of infected farms were comparable to culling if the efficacy level was high enough. For example, ring vaccination with 100 % vaccine efficacy resulted in 95% predicted number of the infected farms of 23, which was equivalent to the culling with 7 delayed days (Table 6.6). These two measures were cheaper than culling, given similar outcomes. Isolation with the best parameter setting was the cheapest measure. However, the range of the indirect costs from isolation was large. For example, for the isolation with a cut-off distance of 0 km and 50% kernel reduction, the median indirect cost was 31.2 thousand euros, but the 95% predicted indirect cost was 338.7 thousand euros, which exceeded the 95% predicted total cost from the baseline. For the ring vaccination, the range of the indirect costs was small, and the median total costs were always lower than the baseline, even with low vaccine efficacy.

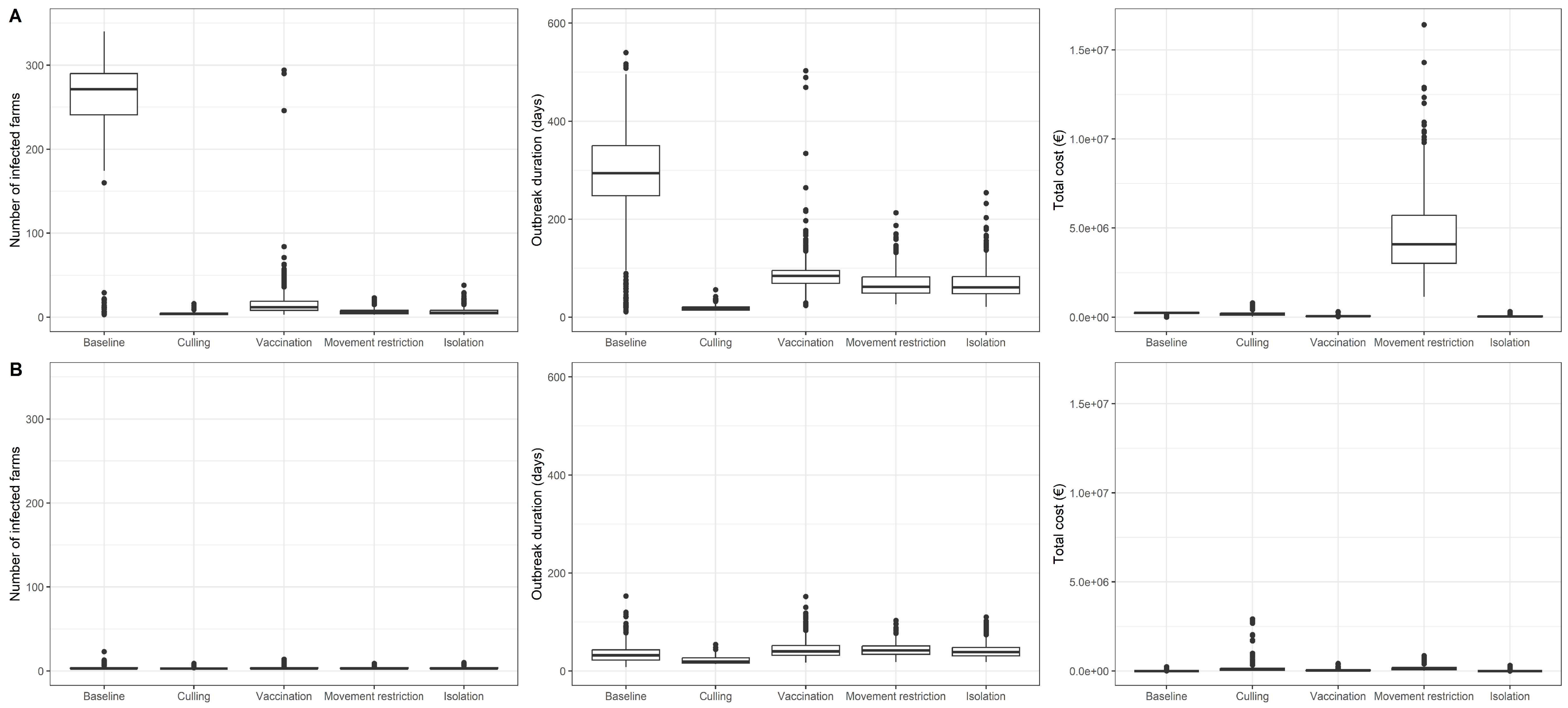

Figure 6.2 The predicted number of infected farms, outbreak duration and total outbreak costs from the simulation of foot and mouth disease outbreaks under the scenarios of baseline without control measures and four control measures (A) the simulation from Lamphaya Klang subdistrict and (B) the simulation from Bo Phloi district.

Table 6.6 Epidemiological and economic indicators for different control measures for simulated foot and mouth disease outbreaks in Lamphaya Klang subdistrict

Control measures	Efficacy level	No. of infected farms [a]		No. of affected farms from control measures [b]		Outbreak duration (days)		Direct costs (thousand €)[c]		Indirect costs (thousand €)	
	Percentile	50	95	50	95	50	95	50	95	50	95
Baseline	-	272	310	-	-	294	442	231.6	235.5	-	-
Culling all animal in infected farms	1 delayed day	4	7	4	7	18	30	0	0.1	145.1	395.7
	7 delayed days	7	29	7	26	38	94	0.7	3.9	238.8	1,270
	14 delayed days	32	156	18	96	113	296	11.8	55.9	978.2	5,239.2
Ring vaccination	100% vaccine efficacy	10	23	481	502	75	109	8.9	23.9	48.7	50.9
	75% vaccine efficacy	12	34	481	502	91	165	11.2	35.4	48.7	50.9
	50% vaccine efficacy	24	257	481	502	140	536	22.5	234.2	48.7	50.9
	25% vaccine efficacy	187	278	481	502	327	565	173	249.7	48.7	50.9
Isolation of infected farms	Cut-off 0 km, 75% kernel reduction	5	16	5	16	61	134	1.6	5.6	17.9	71.7
	Cut-off 0 km, 50% kernel reduction	9	83	9	83	83	282	2.9	29.7	31.2	338.7
	Cut-off 1 km, 75% kernel reduction	21	149	21	149	139	400	7.2	52.7	78.7	632.3
	Cut-off 1 km, 50% kernel reduction	110	217	109	215	259	488	36.7	75.2	413.6	889.2

[a] No. of infected farms including three index cases

[b] No. of affected farms from control measures implies to culled farms in culling, vaccinated farms in vaccination, and isolated farms in isolation, including three index cases

[c] Prices were originally collected in Thai baht (Thai currency) and converted into euro using the study period's average exchange rate of 35.7 Thai baht/euro

The effect of farmers' compliance

The outbreak consequences under different control scenarios and compliance levels are shown in Table 6.7.

Table 6.7 Epidemiological and economic outcomes for different control measures with different compliance levels for simulated foot and mouth disease outbreaks in Lamphaya Klang subdistrict

Control measures	Com-pliance level	No. of infected farms [a]		No. of affected farms from control measures [b]		Outbreak duration (days)		Direct costs (thousand €)[c]		Indirect costs (thousand €)	
	Percentile	50	95	50	95	50	95	50	95	50	95
Baseline	-	272	310	-	-	294	442	231.6	235.5	-	-
Culling with 1 delayed days	100%	4	7	4	7	18	30	0	0.1	145.1	395.7
	75%	5	23	4	17	28	100	0.6	7.5	166.5	860.4
	50%	7	90	4	45	56	248	3	47.9	196.3	2,367.9
	25%	65	234	20	61	210	437	41.6	163.5	899	3,330.8
Culling with 7 delayed days	100%	7	29	7	26	38	94	0.7	3.9	238.8	1,270
	75%	10	84	7	56	61	214	3.2	31.4	333.8	3,044.5
	50%	28	187	13	80	137	370	15	104.3	661.1	4,343.3
	25%	186	264	40	59	266	448	133.1	190.2	2,065.2	3,334
Ring vaccination with 100% vaccine efficacy	100%	10	23	481	502	75	109	8.9	23.9	48.7	50.9
	75%	11	28	361	376	86	155	10.2	29.9	36.5	38.6
	50%	19	245	242	253	115	503	16.9	221.6	24.3	26.2
	25%	128	278	124	129	261	569	117.4	248.4	12.2	13.6
Ring vaccination with 50% vaccine efficacy	100%	24	257	481	502	140	536	22.5	234.2	48.7	50.9
	75%	40	272	361	376	172	565	36.4	242.9	36.3	38.7
	50%	176	283	242	253	321	563	160.9	254.8	24.4	26.3
	25%	231	286	124	129	335	523	209.5	257.2	12.1	13.5
Isolation cut-off 0 km, 75% kernel reduction	100%	5	16	5	16	61	134	1.6	5.6	17.9	71.7
	75%	7	52	5	37	75	218	3.1	28.3	19.6	166
	50%	18	161	9	80	120	397	10.7	105.7	37.9	323.3
	25%	164	254	40	63	266	477	124.3	196.1	149.9	258.3
Isolation cut-off 0 km, 50% kernel reduction	100%	9	83	9	83	83	282	2.9	29.7	31.2	338.7
	75%	24	159	18	118	145	416	11.9	82	69.2	494.6
	50%	99	231	50	115	255	480	59.9	146.3	176.1	485.5
	25%	221	279	56	72	306	475	168.5	213.2	204.6	291

[a] No. of infected farms excluding three index cases

[b] No. of affected farms from control measures implies to culled farms in culling, vaccinated farms in vaccination, and isolated farms in isolation, including three index cases

[c] Prices were originally collected in Thai baht (Thai currency) and converted into euro using the study period's average exchange rate of 35.7 Thai baht/euro

The level of compliance significantly affected the effect of control measures. Less effective control measures required high compliance levels to successfully limit the outbreak. For instance, for culling, with a delay of 1 day, a compliance level of 50% was sufficient to limit the number of infected farms. However, with a delay of 7 days, 100% compliance was necessary to achieve the same outcomes. The boxplots of the number of infected farms, outbreak duration and total costs are presented in Figure 6.3 to visualise the effect of compliance level and control measures.

With lower levels of compliance, the control measures became less effective, leading to a higher number of infected farms and longer outbreak duration, as well as higher total costs (Table 6.7 and Figure 6.3). However, in the case of culling and isolation, measures that had high indirect costs, if control measures could not significantly reduce the outbreak size and duration, a low compliance level resulted in reducing total costs due to less expenditures from fewer compliant farms (Figure 6. 3 and Figure 6.4).

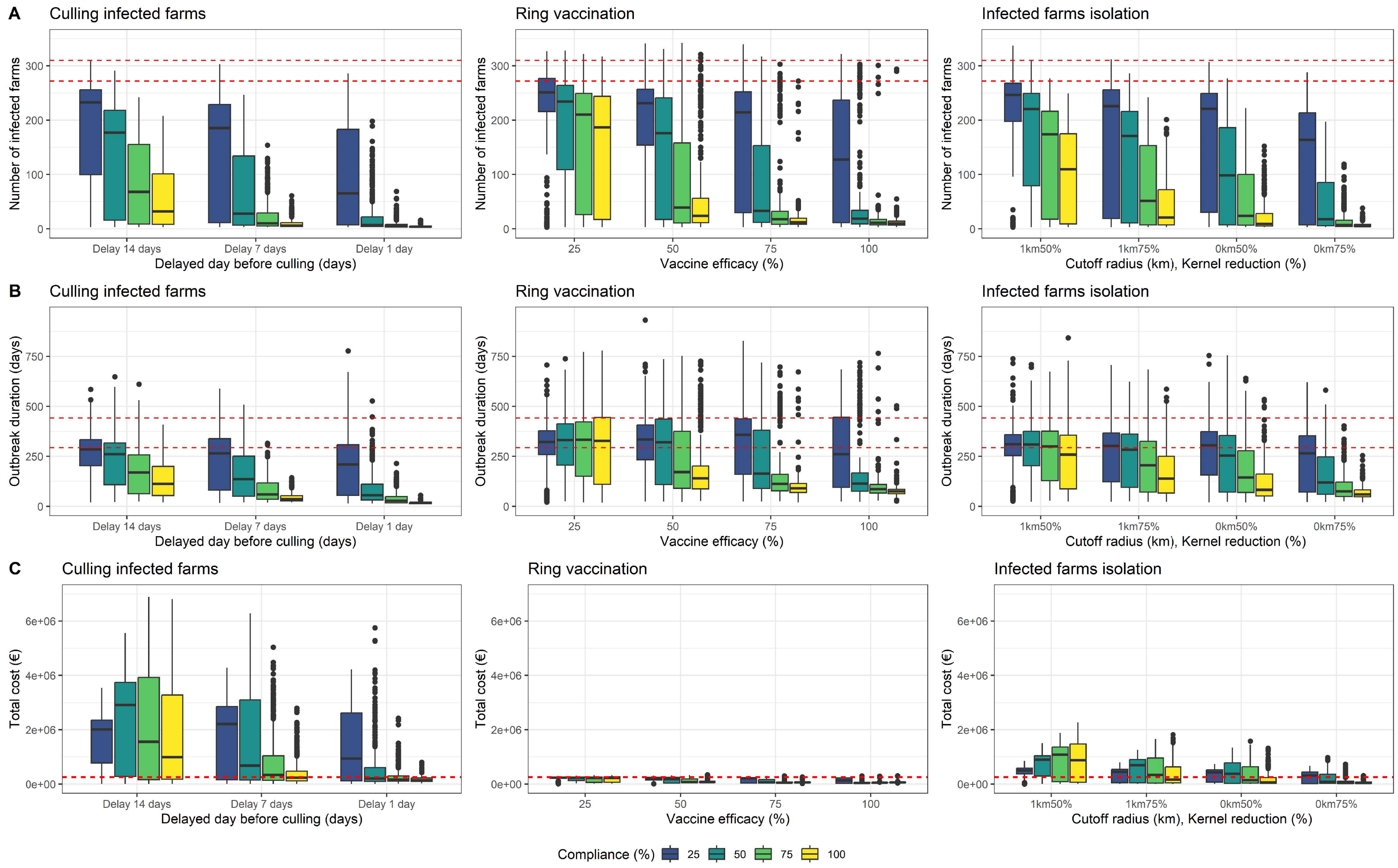

Figure 6.3 Simulation results from Lamphaya Klang subdistrict with different foot and mouth disease control measures efficacy and compliance percentage. (A) the number of infected farms, (B) outbreak duration and (C) total cost. The dashed lines represent the median and 95% prediction from baseline without control measures

Cost distribution between stakeholders

The cost distribution between farmers and the government from different control measures and compliance levels in Lamphaya Klang subdistrict is presented in Figure 6.4.

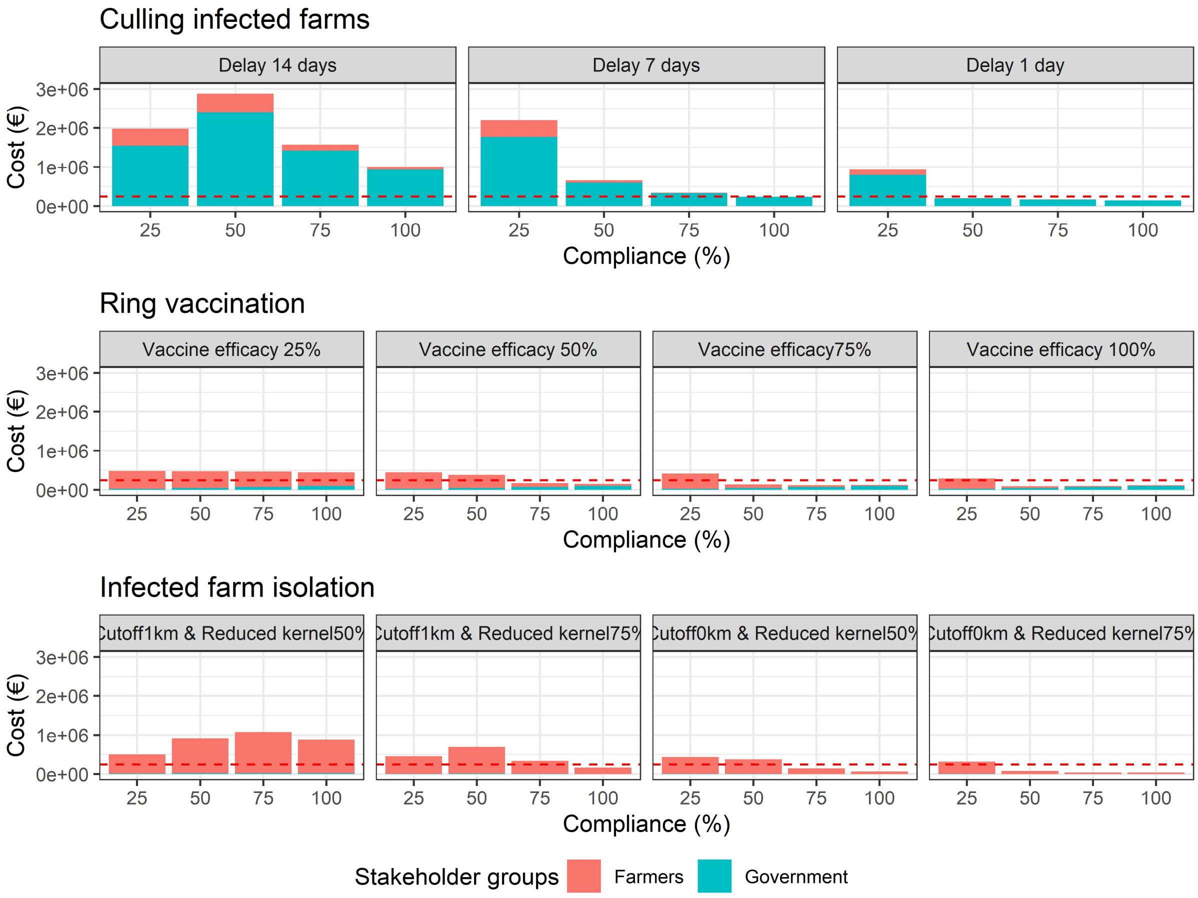

Figure 6.4 Cost distribution between government and farmers for different control measures and compliance levels from Lamphaya Klang subdistrict. The dashed line represents the predicted median total cost from the baseline without control measures.

More than 95% of culling cost was covered by the government. The costs for both government and farmers increased with a long delay (14 days) before culling in combination with a low compliance level. For the isolation of infected farms, farmers bore most of the expenses. In terms of the cost distribution for ring vaccination, a lower compliance level resulted in lower government expenses due to less vaccination, but the costs for farmers were higher from the higher number of infected farms. The costs for farmers were divided and calculated as the average cost per compliant farm and non-compliant farm for each control measure (Table 6.8).

Table 6.8 The average cost for compliant and non-compliant farms from the simulation in Lamphaya Klang subdistrict

Control measures	Average cost for compliant farms (€ per farm) (ratio to baseline)				Average cost for non-compliant farms (€ per farm) (ratio to baseline)			
Compliance (%)	100%	75%	50%	25%	100%	75%	50%	25%
Baseline					484.7[a] (ref.)			
Culling Delay 1 day	128.8 (0.26)	521.5 (1.07)	1374.1 (2.83)	5,464.6 (11.27)	-	1.1 (0.002)	6.0 (0.01)	86.9 (0.18)
Culling Delay 7 day	530.1 (1.09)	1,231.4 (2.54)	3,466.9 (7.15)	6,858.1 (14.15)	-	6.5 (0.01)	30.7 (0.06)	289.3 (0.6)
Ring vaccination 100% efficacy	11.6 (0.02)	9.7 (0.02)	9.7 (0.02)	36.2 (0.07)	-	42.1 (0.09)	53 (0.11)	296 (0.61)
Ring vaccination 50% efficacy	40.6 (0.08)	58.5 (0.12)	275.6 (0.57)	320.2 (0.66)	-	111.3 (0.23)	359.4 (0.74)	437.6 (0.9)
Isolation cut-off 0 km, 75% kernel reduction	3,580.6 (7.39)	3,569.9 (7.37)	3,939.3 (8.13)	3,953.8 (8.16)	-	2.5 (0.01)	15.6 (0.03)	239.5 (0.49)
Isolation cut-off 0 km, 50% kernel reduction	3,624 (7.48)	4006.2 (8.27)	3,900.8 (8.05)	4003.7 (8.26)	-	10.4 (0.02)	93.2 (0.19)	335.2 (0.69)

[a]Average cost per farm for the baseline was calculated from the total cost divided by all farms in the area.

The average cost per farm from the baseline situation were 484.7 euros. The non-compliant farms in the scenario with control measures always paid less than the baseline scenario without control measures. The benefit of non-compliant farms decreased when the efficacy of control measures was lower or when compliance levels were lower. Meanwhile, the compliant farms always paid more than the baseline, except for ring vaccination and the culling with delay of 1 day with 100% compliance. For culling, the delay of 7 or 14 days or low compliance levels led to high cost for compliant farms because of the long outbreak duration leading to a long idle production period. For the ring vaccination, the average cost for compliant farms was lower than for the non-compliant farms, but the difference was less when the vaccine efficacy and compliance level were lower. For the isolation of infected farms, the average cost for compliant farms was almost the same (approximately 8 times higher than the baseline) in all scenarios, but the non-compliant farms gained less benefit when the compliance level and kernel reduction were low.

Discussion

This study aims to evaluate the control measures for FMD outbreaks in Thailand using bioeconomic modelling. To our knowledge, only one study from Perry et al. (1999) evaluated FMD control measures in Thailand with bioeconomic modelling, which was twenty years ago, and the model was simplified, excluding spatial and other heterogeneities. Our novel bioeconomic model did not only update the epidemiological and economic data but focused on outbreak control at the local level and included the factors concerning disease transmission, i.e. the spatial elements of the farms, farm size and farm types. These inclusions reflect the heterogeneity of disease transmission and control measures' effect in different areas. Moreover, our model included the effect of farmers' compliance, which was mostly overlooked in other studies. From the literature review, we found one study from Dürr et al. (2014) that included farmers' compliance with animal movement restrictions. However, this study did not investigate the economic consequences of farmers' compliance. Therefore, our model is novel in terms of examining the effects of farmers' compliance on economic consequences.

Our bioeconomic model allows the comparison of the outbreak control between low-farm-density and high-farm-density area. The outbreaks in the low-farm-density area were small even without intervention, and costs of the implementation of control measures were much more than the reduction in costs of the outbreak. However, these results do not imply that control measures can be disregarded in this kind of area. There is also a probability that FMD transmits to other areas. Those effects were not taken into account. In the high-farm-density area, the outbreaks were big without intervention, and rigorous control measures were necessary for outbreak control. Given the best parameter assumption, all four control measures could limit the outbreak size and duration but resulted in various economic effects. Animal movement restrictions were exceptionally more expensive than other measures. Therefore, the enforcement of animal movement restrictions alone might not be a practical option.

In the bioeconomic model that we developed, the outbreaks were simulated under different efficacy levels of measures to test the uncertainty of control measures' effect.

Culling with the delay of 1 day was the best option in terms of limiting the number of infected farms and outbreak duration, but we noted that this assumption of culling 1 day after detection is hardly achievable in reality. Moreover, the cost of culling was markedly higher than ring vaccination and isolation. The best option for outbreak control from an epidemiological perspective, might not be the best from an economic perspective. Hence, the trade-off between outbreak control and economic returns must be considered. Based on the results, the isolation of infected farms with a cut-off 0 km and 75% kernel reduction had the lowest median predicted cost. However, the prediction interval of the cost was broad, indicating that the cost may become high. Overall, the ring vaccination was the most optimal option in terms of costs since the indirect cost was constant, and the median total costs were always lower than the baseline in every scenario.

Decisions on the control measures should be aligned with the goal of disease control. Thailand is currently mainly focused on reducing outbreak incidences and aims further to eradicate FMD in the selected zone (WOAH, 2022b). In the short and middle term, since the incidences of outbreaks are still high, the resources are insufficient for controlling the outbreaks in every area. The outbreaks in high-farm-density areas should be prioritised, and it might be preferable to use less expensive control measures like ring vaccination and isolation. In the long term, once outbreak occurrences become less frequent and the goal is shifted to disease eradication, effective control measures, like culling, may be implemented to ensure prompt outbreak control.

Numerous studies on farmers' compliance have been done, but they focused mainly on the farmers' perspective and were descriptive surveys (Delgado et al., 2012, 2014; Jemberu et al., 2015; Pham et al., 2017; Young et al., 2014). In this study, we took another approach by estimating the effect of farmers' compliance on the consequences of the outbreak. Based on our findings, the farmers' compliance greatly affected the effect of control measures. We showed an interaction between the efficacy of control measures with compliance. A lower efficacy of the control measure required a high compliance level to control the outbreak and vice versa. Even though the best outcomes were achieved when the compliance level was perfect, in reality, perfect compliance is rarely attainable. Free riders who exploit public goods without contribution may arise (Yong & Choy, 2021). Free riding seems to be rational since our simulation shows that non-compliers are always better off than compliers. Over time, the absence of actions to prevent free-riding will encourage individuals toward non-cooperation (Perc et al., 2017) and leads to the failure of outbreak control. It is important to comprehend farmers' incentives to prevent free-riding.

The cost distribution between stakeholders should be considered when making decisions. For instance, the culling required huge expenses from the government. Hence, it might not be feasible if the government has an inadequate budget. On the contrary, the isolation costs were mostly paid by farmers. It implies that farmers may not be incentivised to follow the isolation, leading to low compliance. In addition, the comparison of cost distribution between compliant and non-compliant farms could determine farmers' compliance. Those control measures that demand high contributions from compliant farmers, such as culling and isolation, may advocate free-riding. On the other hand, the ring vaccination may entice farmers to comply due to the benefit gained by compliant farms.

Regarding policy implication, our results provide information for local authorities to customise FMD control measures based on their areas. Even though the model only focused on two areas of Thailand, the results can be applied to other areas with a similar situation, particularly for the results from Lamphaya Klang subdistrict, which is a representative of areas with high-density of dairy farms. Approximately 60% of dairy cattle are located in densely populated areas in four provinces in the central region of Thailand (Department of Livestock Development (DLD), 2020). Therefore, the model could be applied to the subdistricts in these provinces, which are inhabited by half of the dairy population in Thailand. The success of outbreak control was highly dependent on the farmers' compliance. It is important that the government takes actions to incentivise farmers, such as offering reasonable compensation for culled animals (Pham et al., 2017), supporting free-of-charge FMD vaccine (Jemberu et al., 2015) and good outbreak communication (Delgado et al., 2014). Further research should be conducted on the perspectives of the farmers to gain more information for policy planning.

Despite our best effort to develop a representative bioeconomic simulation model, some simplifications were used for the economic calculations. Only the direct costs from production losses and the indirect costs from the implementation of control measures were calculated, but the revenue forgone and the market effect were not taken into account. However, the main goal of this study was not to calculate the exact costs of outbreak control, but to study the effect of control measures and farmers' compliance. The model already accounted for the uncertainty regarding the efficacy of control measures and compliance level. In addition, we made a few suggestions for future research. First, in this study, the control measures were individually applied in each scenario. However, in reality, several measures are usually implemented together to control the outbreak. Second, to keep the model updated with current situation, the parameters should be derived from recent outbreak and economic data. Third, due to the small scale of the model (subdistrict level), the effect on the market and price changes did not matter and was not considered in the model. However, if the model was expanded to large scale (regional or country level), the market and price changes will highly affect the economic input and should be considered in the model.

Conclusion

The requirement of control measure level differed between the low-farm-density area (Bo Phloi) and the high-farm-density area (Lamphaya Klang). In the low-farm-density area, the measures could be more lenient due to small outbreaks. On the contrary, in high-farm-density area, the measures needed to be strict to successfully control the outbreak. The total cost of outbreak control varied, depending on the area and the control measures. From the simulation, animal movement restrictions are not a practical option due to their exceptionally high cost. Culling was the best option for outbreak control from an epidemiological perspective, but it was costly. The isolation of infected farms could control the outbreak and reduce the costs. However, the outcome was uncertain, and the costs could be high. From an economic perspective, ring vaccination was the best option, given similar outcomes. Farmers’ compliance was an important factor to take into account. Insufficient farmers' compliance led to the failure of outbreak control and increased outbreak costs compared to the situation without intervention. The measures that incur high costs on the compliant farms, such as culling and isolation, might result in low compliance. In contrast, ring vaccination, which provided benefit for compliant farms, might get a high level of compliance from farmers. The results of this bioeconomic simulation study provide insight into the effect of control measures and farmers' compliance and information for designing appropriate control measures in distinct areas.

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Supplementary materials

Supplementary S6.1 Additional results

Table S6.1.1 Summary the simulation results in Lamphaya Klang subdistrict

Control measures	Parameters	Number of secondary infected farms		Outbreak duration (days)		Number of affected farm from control measures[a]		Total costs (thousand €)[c]	
	Percentiles	50%	95%	50%	95%	50%	95%	50%	95%
Baseline	-	272	310	294	442	-	-	231.6	261.0
Culling infected farms	Delay 1 day	4	7	18	30	4	7	138.2	376.7
	Delay 7 days	7	29	38	94	7	26	228.7	1212.6
	Delay 14 days	32	156	113	296	18	96	944.2	5041.0
Ring vaccination	100% vaccine efficacy	10	23	75	109	481	502	54.5	70.2
	75% vaccine efficacy	12	34	91	165	481	502	56.5	78.1
	50% vaccine efficacy	24	257	140	536	481	502	67.2	267.2
	25% vaccine efficacy	187	278	327	565	481	502	210.6	283.7
Animal movement restriction	Cutoff distance 0km + 75% kernel reduction	6	16	62	117	-[b]	-[b]	4084.0	8573.7
	Cutoff distance 0km + 50% kernel reduction	11	64	97	271	-[b]	-[b]	6901.9	21170.4
	Cutoff distance 1km + 75% kernel reduction	19	103	128	341	-[b]	-[b]	9434.1	26900.3
	Cutoff distance 1km + 50% kernel reduction	65	200	235	469	-[b]	-[b]	18258.2	37360.1
Infected farms isolation	Cutoff distance 0km + 75% kernel reduction	5	16	61	134	5	16	36.3	142.4
	Cutoff distance 0km + 50% kernel reduction	9	83	83	282	9	83	62.6	684.6
	Cutoff distance 1km + 75% kernel reduction	21	149	139	400	21	149	160.8	1276.0
	Cutoff distance 1km + 50% kernel reduction	110	217	259	488	109	215	836.2	1790.3

[a] Number of affected farms from control measures implies culled farms in culling, vaccinated farms in vaccination, and isolated farms in isolation, including three index cases.

[b] All farms in the area were under animal movement restrictions.

[c] Prices were originally collected in Thai baht (Thai currency) and converted into euro using the study period's average exchange rate of 35.7 Thai baht/euro

Table S6.1.2 Summary the simulation results in Bo Phloi district

Control measures	Parameters	Number of secondary infected farms		Outbreak duration (days)		Number of affected farm from control measures[a]		Total costs (thousand €)[c]	
	Percentiles	50%	95%	50%	95%	50%	95%	50%	95%
Baseline	-	3	10	32	89	-	-	0.9	108.8
Culling infected farms	Delay 1 day	3	6	19	34	2	5	65.7	864.9
	Delay 7 days	3	7	24	47	2	4	60	877
	Delay 14 days	3	7	29	58	1	3	39.3	403.7
Ring vaccination	100% vaccine efficacy	3	7	40	78	167	276	35.6	141.1
	75% vaccine efficacy	3	8	41	82	167	285	35.6	155.1
	50% vaccine efficacy	3	8	40	83	169	285	33.7	189.5
	25% vaccine efficacy	3	9	40.5	87	170	287	37.3	189.8
Animal movement restriction	Cutoff distance 0km + 75% kernel reduction	3	6	42	75	-[b]	-[b]	111.4	458.7
	Cutoff distance 0km + 50% kernel reduction	3	7	41	84	-[b]	-[b]	112	427.9
	Cutoff distance 1km + 75% kernel reduction	3	7	41	78	-[b]	-[b]	105.1	548.9
	Cutoff distance 1km + 50% kernel reduction	3	8	42	85	-[b]	-[b]	109.3	569.5
Infected farms isolation	Cutoff distance 0km + 75% kernel reduction	3	6	22	39	3	5	2.1	100.3
	Cutoff distance 0km + 50% kernel reduction	3	7	23	39	3	5	2.1	171.7
	Cutoff distance 1km + 75% kernel reduction	3	7	22	40	3	6	2.1	101.8
	Cutoff distance 1km + 50% kernel reduction	3	8	23	41	3	6	2.2	106

[a] Number of affected farms from control measures implies culled farms in culling, vaccinated farms in vaccination, and isolated farms in isolation, including three index cases.
[b] All farms in the area were under animal movement restrictions.
[c] Prices were originally collected in Thai baht (Thai currency) and converted into euro using the study period's average exchange rate of 35.7 Thai baht/euro

Supplementary S6.2 Economic calculation

For the FMD economic calculation, the economic losses comprise direct costs from production losses and additional costs from the implementation of control measures. The parameters were retrieved from multiple sources, including literature, farmer interview data from 4 districts of Thailand and experts' opinions (i.e. local veterinarians and local government officers). Since the data on the number of animals specified by age categories are not available for all farms, we estimated the number of animals in each age category by multiplying farm size with the average herd composition. Here, we present the costs in Thai baht. It should be noted that the exchange rate during the study period was 35.7 Thai baht to 1 euro. The detail on cost calculations by stakeholders and scenarios are explained below. The detailed calculation can be found in:

https://doi.org/10.5281/zenodo.7890415

Supplementary S6.3 R code for simulation

The R code for simulation model can be found in https://doi.org/10.5281/zenodo.7708619


7

Chapter 7

General Discussion

Introduction

Foot and mouth disease (FMD) is a highly contagious viral disease that affects cloven-hoofed animals, including cattle, pigs, sheep, goats and buffaloes (Davies, 2002). FMD causes significant economic losses to livestock production due to production losses, trade restrictions, and costs of disease control measures (James et al., 2002; Knight-Jones et al., 2017; Knight-Jones & Rushton, 2013). In Thailand, FMD is a significant livestock disease, particularly among dairy cattle, where it negatively impacts milk production and leads to considerable economic losses for dairy farms (Suriya, 2015). Additionally, FMD is a major obstacle to Thailand's pig production sector in terms of international pork exports (Tantasuparuk & Kunavongkrit, 2015). To address this, the Thai government has actively participated in the Progressive Control Pathway for FMD (PCP-FMD) (FAO, 2018). Presently, Thailand has reached stage 3 in the PCP-FMD, indicating regular reporting of FMD incidence and the establishment of formal regulations for FMD control (FAO, 2018).

While Thailand has implemented several measures, such as premises quarantine, emergency vaccination, and animal movement restrictions, FMD outbreaks continue to occur every year (Blacksell et al., 2019; Punyapornwithaya et al., 2022; WOAH, 2022a). High incidence of outbreaks highlights the need for improvement in current FMD control measures to maintain current PCP-FMD stage and progress to the next stage, which is achieving FMD-free status with vaccination. Effective FMD control measures require support from solid epidemiological and economic information. However, there is a lack of such information regarding FMD control measures in Thailand. This issue leads to the main objective of this thesis: to gather epidemiological and economic information on FMD outbreaks in Thailand and to evaluate the effectiveness of FMD control measures.

In this general discussion, first, all results are synthesised. Second, data and methodological approaches are discussed. Third, policy implications, based on the findings of this thesis are indicated. Fourth, future research outlooks are suggested, and the last, main points of thesis are concluded.

Synthesis of the results

This section provides a synthesis of the results from Chapters 2-6, which are divided into two interconnected parts. The first part of this thesis (Chapters 2 - 4) focuses on acquiring information on the epidemiology and economics of FMD outbreaks in Thailand. The second part (Chapters 5-6) focuses on assessing FMD control measures through cost-effectiveness analysis, utilising the information obtained in the first half.

Epidemiology and economics of FMD outbreaks in Thailand

Acquiring robust epidemiological and economic data is crucial to support effective disease control efforts. While there has been considerable research conducted on epidemiology and economics of FMD in Thailand (Arjkumpa et al., 2020a, 2020b; Sansamur et al., 2020), further research is required due to distinct behaviour of outbreaks influenced by local circumstances. Additionally, the endemic situation in Thailand presents a unique scenario that has not received adequate attention in previous studies. Given that policy decisions for FMD control should be strategically planned at national, local, and farm levels, the information regarding the disease should be comprehensively gathered at each level. To address this issue, my thesis employed a top-down approach, starting from the national level and gradually delving into subdistrict and farm levels, to gain insight into FMD outbreaks in Thailand at every level.

In analysing FMD outbreaks at the country level, we used national outbreak data from from 2011 to 2018, including all types of livestock. This broader perspective sets it apart from previous studies that focused on specific regions and solely included outbreaks in cattle (Arjkumpa et al., 2021; Chamnanpood et al., 1995; Cleland et al., 1996; Sansamur et al., 2020). The data was analysed in multiple aspects, including temporal and spatial patterns and risk factors. A total of 826 FMD outbreaks were reported in 564 subdistricts out of the 7,425 subdistricts in Thailand from 2011 to 2018 (Chapter 2). The temporal analysis showed that the outbreak incidences reached the annual highest peak in October and November. These results correspond with the results reported in another study. (Punyapornwithaya et al., 2022). Spatial analysis demonstrated a heterogeneous distribution of outbreaks throughout the country, with several clusters identified in the central, southern, and northern regions. Most clusters were small and localised, limited to a few subdistricts. These findings indicate that the probability of FMD outbreak occurrence in each area is not equal, with certain areas posing a higher risk of outbreaks than others. Risk factor analysis identified several risk factors related to FMD outbreak occurrence, including an increase in the cattle and pig population, international border, livestock market and the occurrence of FMD outbreak in an adjacent area. The integration of several techniques for temporal, spatial, and risk factor analysis provides an overall big picture of FMD outbreaks in Thailand, revealing where, when, and why the outbreaks occur.

Since FMD outbreaks in Thailand mostly occur locally within few adjacent subdistricts (Chapter 2), outbreak control management should be focused at the subdistrict level. The first step in planning outbreak control within a subdistrict is to understand the transmission dynamics between farms during an outbreak. For this purpose, the concept of spatial transmission kernel was utilised to estimate the between-farm transmission rate. The spatial transmission kernel is a function of the between-farm transmission rate and the distance between the farms. This approach allows the inclusion of spatial factors in estimating the transmission rate. While the use of transmission kernels is common in studies conducted in FMD-free countries, it had not been previously applied in an endemic situation. Therefore, in chapter 4, we addressed this gap. The estimation was based on outbreak data from Lamphaya Klang subdistrict in 2016. The transmission rate during the FMD outbreak in Thailand (transmission rate at 0 km = 0.0054 day^{-1}) was higher than the transmission rate in FMD-free countries, such as in the Netherlands (transmission rate at 0 km = 0.0018 day^{-1}) (Boender et al., 2010) and in Japan (transmission rate at 0 km = 0.00074 day^{-1}) (Hayama et al., 2013) and rapidly declined over shorter distances. This spatial transmission kernel indicated a high risk of infection within close proximity to infected farms. Therefore, the control measures should be focused in close proximity to infected farms. Notably, the susceptibility and infectivity increased with larger farm sizes, indicating that during outbreak control, particular attention should be given to large farms to minimise disease spread. Additionally, including distance-independent transmission parameters improved the model fit. This implies that additional transmission routes, that are not dependent on between-farm distance, might be presented during the outbreak, such as contacts between free-grazing cattle and contamination by traders and feed trucks. These findings highlight the importance of considering these transmission routes for the implementation of measures.

Understanding the impacts of FMD at the farm level is crucial in making informed decisions regarding FMD control measures, as it serves as a basis for weighing the effectiveness and feasibility of various control options. Moreover, farmers often demonstrate a greater willingness to comply with control measures when they perceive the benefit of the implementation. Providing farmers with insight into FMD losses can serve as a powerful motivator to encourage their participation in FMD control. To estimate the epidemiological and economic impacts at the farm level, in Chapter 3, we used interview data collected from FMD-affected farms in four districts in Thailand. Morbidity and mortality rates of FMD at the farm level were calculated. The findings show that the morbidity rates in the same species were significantly different between areas. The morbidity rates also significantly differed between each animal age category, with the lowest morbidity rate observed in calves. These findings indicate that the severity of the disease varies across different areas, animal species and age categories, as supported by previous studies (Megersa et al., 2009; Nyaguthii et al., 2019; Sangrat et al., 2020; Yano et al., 2018). Regarding the economic impacts, the economic losses of FMD on dairy farms were estimated using the farm-specific mortality and morbidity data, in combination with information on farm size and specific estimates of loss parameters obtained through farmer interviews. The most significant losses were the decreased milk production (mean = 1,063, min = 6 and max = 14,688 USD per farm), followed by mortality losses (mean = 532, min = 0 and max = 6,286 USD per farm). On average, the economic losses per FMD outbreak was estimated to be 2,454 USD per farm (with a minimum of 79 USD and a maximum of 17,720 USD per farm), or 56 USD per animal (with a minimum of 2 USD and a maximum of 377 USD per animal). These losses accounted for approximately one-third of the annual profit per animal. (Suriya, 2015). These findings indicated variations in the impacts of FMD at the farm level and highlighted the potential for significant economic consequences on farms.

Evaluation of FMD control measures in Thailand

The analyses of FMD outbreaks in Thailand reveal an uneven occurrence of FMD outbreaks in different areas of Thailand (Chapter 2). Within a subdistrict itself, the probability of infection between farms was also different depending on farm density (Chapter 4). Moreover, the economic losses of FMD per farm varied between different areas and farm types (Chapter 3). All of these findings highlight the heterogeneity of FMD outbreaks, making it a complex issue to deal with. It implies that the current general "one-size-fits-all" control measures might not be appropriate for all areas, and instead, control measures should be customised in order to align with the specific conditions of each affected area. Therefore, in Chapters 5 and 6, we conducted an evaluation of FMD control measures in two distinct areas with varying conditions to demonstrate the differential effects of control measures under different circumstances.

In Chapter 5 of this thesis, we focused on assessing the epidemiological outcomes of control measures using a stochastic between-farm transmission model. The model was used to simulate FMD outbreaks in two subdistricts with different settings: high and low-farm density. The parameters for between-farm transmission rate were derived using the spatial transmission kernel method as explained in Chapter 4. Moreover, the model also incorporated the input from epidemiological data from Chapters 3, such as farm location, farm types and farm size to reflect the different conditions of areas. Multiple FMD control measures were tested as scenarios with the model to reflect their effects under different conditions. The control measures included standard measures used in Thailand, such as ring vaccination, animal movement restrictions, and isolation of infected farms (Arjkumpa et al., 2020b; Yano et al., 2018), as well as uncommon measures like culling animals in infected farms. Based on the simulation, in the low-farm-density area, FMD outbreaks were small with the median number of infected farms = 3 (95% prediction interval of (0, 13)). Hence, such an outbreak could end without any interventions. The implementation of control measures in this area did not have significant epidemiological benefits. In contrast, the outbreaks in the high-farm-density area were big without intervention with the median number of infected farms = 293 (95% prediction interval of (0, 361)). Such outbreaks would continue until the susceptible farms in the area were depleted (Chapter 5). In the high-farm-density area, rigorous control measures, such as culling, provided a significant effect on outbreak control. For example, culling with a delay of 1 day can reduce the number of infected farms to 1 (95% prediction interval of (0, 7)). These findings imply different requirements for control measures in different farm-density areas.

When designing control programs, it is important to consider not only the epidemiological consequences but also the economic consequences to ensure the economic feasibility of the measures (Rich et al., 2005). Therefore, in Chapter 6, we studied the economic consequences of FMD control measures. Simulating control measures in the high-farm-density area under the assumption of 100% efficacy, shows that all measures were effective in limiting the outbreak size and duration, but their implementation incurred different costs. In terms of economic impacts, animal movement restrictions were exceptionally expensive (median total outbreak cost of 4.08 million euros and the average cost per farm of 8,113 euro per farm) compared to the situation without any interventions (median total outbreak cost of 0.23 million euros and the average cost per farm of 484.7 euro per farm). Therefore, the implementation of animal movement restrictions alone was not a practical option. Comparing the epidemiological effectiveness of control measures at their best efficacy, culling was the most effective control option to limit the outbreak size and duration followed by isolation of infected farms and ring vaccination However, the cost of culling was higher compared to ring vaccination and isolation, given their similar outcomes. Overall, ring vaccination proved to be the most cost-effective measure among all options, considering the comparable outcomes in controlling the outbreaks.

Furthermore, the varying probability of outbreak between different areas (Chapter 2 and 3) and the variability in economic losses per farm (Chapter 4) can influence farmers' attitudes towards FMD control, leading to differences in their compliance. While farmers' compliance is an important factor affecting the effectiveness of outbreak control, most studies on FMD outbreak control implicitly assumed 100% compliance, which was rarely the case in reality. For the model in Chapter 6, we took a new approach by including farmers’ compliance in the model and demonstrated the theoretical effect of farmers' compliance on the effect of control measures. The outcomes of control measures were considerably affected by farmers' compliance. In general, control measures with a low efficiency require a high compliance level to successfully control outbreaks, and vice versa. For example, in the case of ring vaccination with a vaccine efficacy of 100%, controlling the outbreaks required a minimum of 50% farmers' compliance. However, if the vaccine efficacy was reduced to 75%, getting the same outcomes would need at least 75% farmers' compliance. Some control measures, like quarantine of infected farms, were highly affected by the compliance level. The results emphasise the need for attention to farmers' compliance when designing control measures.

In addition to assessing the overall economic impact, the distribution of costs among different stakeholders needs to be considered when making decisions. By taking into account the cost distribution, decision-makers can assess the burden of control measures on each stakeholder and estimate the economic incentives for compliance with the measures. Our results showed that each control measure had different cost distributions between stakeholders. For the culling, the government was responsible for most costs. Therefore, if the government's budget was insufficient, the control by culling might not be feasible. In contrast, the isolation that required a high contribution from farmers might lead to low economic incentives for farmers. Non-compliant farms were financially better off than compliant farms for all measures except ring vaccination, indicating a big monetary incentive for farmers to avoid complying with control measures such as isolation.

In summary, the distinction of the outbreak size and its impact in different areas highlighted the importance of customising FMD control measures based on farm density, farm size and farm type. Using bioeconomic modelling for ex-ante analysis of control measures can help to assess the trade-off between outbreak control and economic efficiency. Furthermore, the simulation results provide valuable insight into the potential impact of farmer compliance on outbreak control, emphasising its critical role in the design of effective control measures.

Data and methodological approaches

In this thesis, a number of datasets from multiple sources and various methods from multiple disciplines were used to answer research questions in both epidemiological and economic aspects. A schematic diagram of datasets and methods used in this thesis is shown in Figure 7.1.

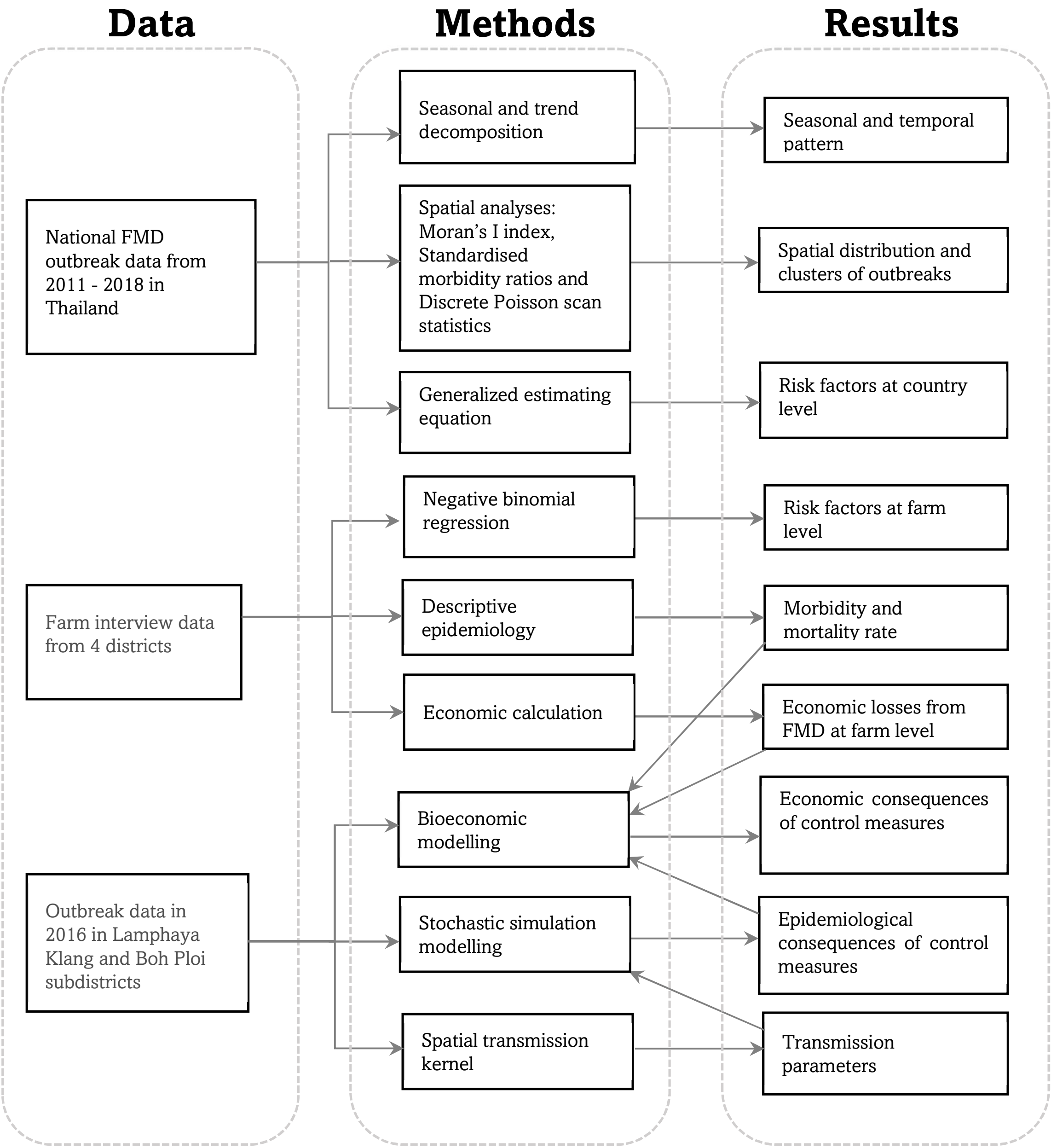


Figure 7.1 A schematic diagram of data and methods used in this thesis. The left column shows datasets from multiple levels (national, subdistrict and farm level). The middle column shows the methods used in this thesis. The right column shows the results. The arrows show the linkage between the datasets, methods and results.

In Chapter 2, we used the data from FMD outbreak reports from the World Animal Health Information System (WOAH, 2022a). Even though Thailand has reported national FMD outbreaks since 2007. These data are mainly used for the annual report without further comprehensive analysis. Further epidemiological analyses have never been conducted despite the available database. We analysed this outbreak data from 2011 to 2018 through multiple quantitative methods, such as seasonal and trend decomposition with locally estimated scatterplot smoothing (Cleveland et al., 1990), discrete Poisson scan statistics (Kulldorff, 2020) and generalized estimating equation logistic regression models (Halekoh et al., 2006). In contrast to previous studies that focused solely on temporal pattern (Punyapornwithaya et al., 2022), spatial pattern (Sangrat et al., 2020), or risk factors (Sansamur et al., 2020), the combination of these approaches in this study provides a comprehensive understanding of overall pattern of FMD outbreaks in Thailand. However, a small remark should be noted on the quality of the data since the data came from a government report, which mainly relies on passive surveillance. It might cause under-reporting (Sangrat et al., 2020).

In Chapter 3, descriptive analyses were used to estimate mortality, morbidity and economic losses based on the FMD-affected farm interview data from 4 subdistricts. Moreover, negative binomial regression (Dunn and Smyth, 2018) was used to identify risk factors. These methods provide knowledge of the epidemiological and economic impacts at the farm level, which was lacking in Thailand. A few limitations on data should be mentioned here. First, the data was collected by using clinical signs as a case definition. This might lead to an underestimation of the prevalence in case of subclinical infection (Buckle et al., 2021). Second, although previous research has demonstrated significant impacts of FMD on intensive pig farms (James and Rushton, 2002), the number of pig farms included in this study is limited. Our results can represent the FMD effects on pig farms in the study areas, but to obtain more generalized findings, additional data from pig farms will be needed in future studies.

In Chapter 4, we obtained the FMD outbreak data in 2016 from farmer interviews conducted in Lamphaya Klang subdistrict. We used this data to study between-farm transmission dynamic. Our study benefited from detailed outbreak data that included farm location, farm size, animal type, and estimated farm infectious period. This detailed dataset allowed us to derive between-farm transmission rates that incorporated the spatial features of farms using the concept of spatial transmission kernel (Boender et al., 2010). This innovative approach provided insights into the transmission dynamics in areas with varying farm densities. However, a limitation of the spatial transmission kernel should be noted. Since the spatial transmission kernel always assumes that the transmission rate is based on the distance between the farms. Therefore, it is not able to represent the non-spatial dependent transmission.

In Chapter 5, we developed the stochastic between-farm simulation model by using the input data from FMD outbreak data in Lampahaya Klang subdistrict and Bo Phloi district. Unlike many transmission models used in endemic areas that rely on historical FMD incidence (Jemberu et al., 2016b; Nampanya et al., 2015; Young et al., 2016). This model brings novelty by incorporating the spatial features of farms through the between-farm transmission rates derived from the concept of the spatial transmission kernel. (Boender et al., 2010). Moreover, the farm size (Boender et al., 2014), farm type (Backer et al., 2012), and animal trade network (Fajardo et al., 2021) were included in the model to enhance the representation of the diverse outbreaks that occur in different areas. Such a complex model is novel for FMD modelling in an endemic situation. However, the limitation of modelling using the transmission kernel method should be noted. The spatial transmission kernel subsumes transmission rates (in a function of distance between farms) from all kinds of transmission routes without distinguishing between the routes. As a result, it becomes challenging to quantify and adjust the effect of control measures on the spatial transmission kernel, particularly when there are only a few studies available that demonstrate the impact of control measures on the transmission kernel. In addition, in Chapter 5, we aimed to address the limitation of the spatial transmission kernel's inability to represent distance-independent transmission by integrating the trade network to account for non-spatial dependent transmission. However, due to incomplete animal trade data, the derived trade transmission parameter did not have significant results. If supplementary data on animal movement and trading would be available, incorporating this data could enhance the model simulation and provide a more accurate reflection of the situation. It should be noted that our models only focus on two study areas due to the availability of data. The general application of spatial transmission kernels in other areas is limited by the lack of comprehensive outbreak data to derive parameters in other subdistricts. Additional outbreak data from other areas with different animal species and farm densities can help to generalise the model further.

In Chapter 6, the bioeconomic model for assessing FMD outbreak control was developed by combining the stochastic transmission model from Chapter 5 and economic data from Chapter 3. Moreover, we bring a novelty to this model by including the uncertainty of farmers' compliance. Most studies on farmers' compliance were focused on qualitative surveys or perspectives of farmers (Delgado et al., 2012; Jemberu et al., 2015; Pham et al., 2017; Young et al., 2014). However, in this thesis, another approach was used by modelling the theoretical effect of compliance level on the outcomes of FMD control. The assessment of farmers' compliance in quantitative terms is a unique approach that is not commonly found in other models. It should be mentioned that economic calculations in this model were simplified. Due to the small scale of the model at the district level, price changes due to changes in supply and market effects are not significant and were not included in the model. However, we noted that price changes could potentially impact farmers' compliance. For instance, during periods of high milk prices, farmers may exhibit higher compliance due to increased economic losses, while the opposite may occur during periods of low milk prices. Although this issue was not explored in this study, future research should consider incorporating the economic effect, especially when scaling up the model to larger regions or the entire country.

Policy implications

The findings from this thesis can contribute towards improved disease control measures and advances the progress towards achieving the PCP-FMD stage. Regarding disease control at the national level, the overview of national FMD outbreaks in Chapter 2 can be used to support resource allocation for FMD outbreak control toward high-risk periods and areas. Regarding the policy for routine vaccination, the temporal pattern suggests that the routine FMD vaccination program should be completed a month (Doel, 1996) before October to ensure that the animals develop immunity before the high-risk period (October – November). Due to the high risk of transboundary transmission, strict quarantine measures are necessary at national borders (Wongsathapornchai et al., 2008b). Moreover, the stringency of surveillance in each area could be adjusted based on the probability of outbreak occurrence. Priority should be given to high-risk areas, especially those with a large number of animals and significant animal trade activity. This allocation of resources ensures early detection and prompt outbreak control measures.

Regarding outbreak control at the district level, the findings in Chapters 4 - 6 show the distinct severity of outbreaks depending on farm density, farm type and farm size. It highlights the importance of implementing area-specific control measures rather than relying on general control measures. In areas with high farm densities, FMD outbreaks tended to be more severe. Therefore, it was important to prioritise outbreak control in these areas by implementing strict control measures. On the other hand, in areas with low farm densities, outbreaks were smaller and could sometimes end without intervention. However, minimum control measures were still required to prevent the spread of the outbreak to other areas.

The decision on which control measures to implement should be aligned with the goal of disease control. Currently, Thailand is in stage 3 of PCP-FMD (WOAH, 2017), with the main goals to decrease the incidence of outbreaks and mitigate the impact of the outbreaks that have already occurred. In the current situation, given the high incidence of FMD outbreaks and limited resources available for disease control measures, the outbreak control efforts should prioritise high-farm-density areas where the probability of a big outbreak is greater. Implementing cost-effective control measures such as ring vaccination would be the preferable option (Chapter 6). In the future, as outbreaks become less frequent and the goal shifts towards progressing the PCP-FMD status by eradicating the disease, more efficient measures like culling may be favoured choices (Chapter 6).

Our economic evaluation of FMD outbreaks highlights the substantial economic losses that farms may experience due to FMD (Chapter 3). As a result, the quantification of disease impact can be used to motivate farmers and other stakeholders to participate in FMD outbreak prevention and control programs. The cost distribution between stakeholders implies that some farmers had a significant monetary incentive not to comply. It indicates that policymaking required the provision of incentives that encourage farmers to follow the regulations. These measures may include compensation for culled animals (Pham et al., 2017), free-of-charge FMD vaccine (Jemberu et al., 2015) and effective outbreak communication (Delgado et al., 2014) or imposing penalties, such as fines for unauthorised animal movements, to discourage non-compliance.

Future research outlook

This thesis provides insight into the epidemiology and economics of FMD outbreaks in Thailand and the assessment of control measures. Nevertheless, further research could be conducted to enhance disease control. As new data on national outbreaks are reported annually (WOAH, 2022a), any analysis and models related to national FMD outbreaks should also be updated concurrently to provide an up-to-date overview of the current outbreak situation. We recommended to automate the process and incorporate real-time data concurrently. This would ensure an up-to-date overview of the current outbreak situation. Furthermore, the successful control of FMD requires international collaboration to prevent transboundary transmission (Blacksell et al., 2019), Therefore, it would be advantageous to analyze the data collected by the WOAH reporting system from neighboring Southeast Asian countries as well. Access to up-to-date information on the FMD situation in the region could help Thailand in better preparing for surveillance and implementing control measures in advance.

The modeling in this study is limited to data from only two districts. Further studies are needed to derive transmission parameters in other areas. The modeling approach presented in this thesis can serve as a foundation for a generic framework to update the transmission kernel using additional outbreak data from various subdistrict. This would result in more generalized transmission parameters. With robust transmission parameters and animal census data that includes farm density and species, it will be possible to develop a reproduction number map (Boender et al., 2007). This map is useful in identifying areas that could potentially cause major outbreaks and guide decisions on outbreak control measures.

The model in this thesis focuses on outbreak control in a single area and assesses control measures under such conditions. Further studies should expand the model on a broader scale, taking into account the risk of disease introduction from and into other areas since the decision-making process should not only focus on disease control in one area but consider the larger picture, as well as any potential market effects that may arise (Saatkamp et al., 2016). One of the approach is to use the probability of outbreak occurrences as presented in Chapter 2 to estimate the risk of disease introduction from other subdistricts.

While the economic study presented in this thesis focuses primarily on data from cattle farms, it is important to note that FMD can also have a significant impact on other species. As such, further analysis should be conducted on other species, particularly in pig farms, which play a significant role in Thailand's livestock production (Tantasuparuk and Kunavongkrit, 2015). The main limitation of under-reporting cases in pig farms might be addressed by using Bayesian approach to estimated undetected infectious cases (Jewell et al., 2009).

Apart from the stakeholders involved in this study, such as farmers and the government, future studies should also include other stakeholders in the analysis, such as feed companies, milk collection centres, milk processors, animal traders, and slaughterhouses. These stakeholders play a crucial role in FMD transmission and contribute significantly to the implementation of FMD control measures (Marsot et al., 2014). Conducting additional qualitative studies on stakeholders' perceptions and behaviour could provide valuable insights into how to encourage their willingness to participate in FMD outbreak control measures.

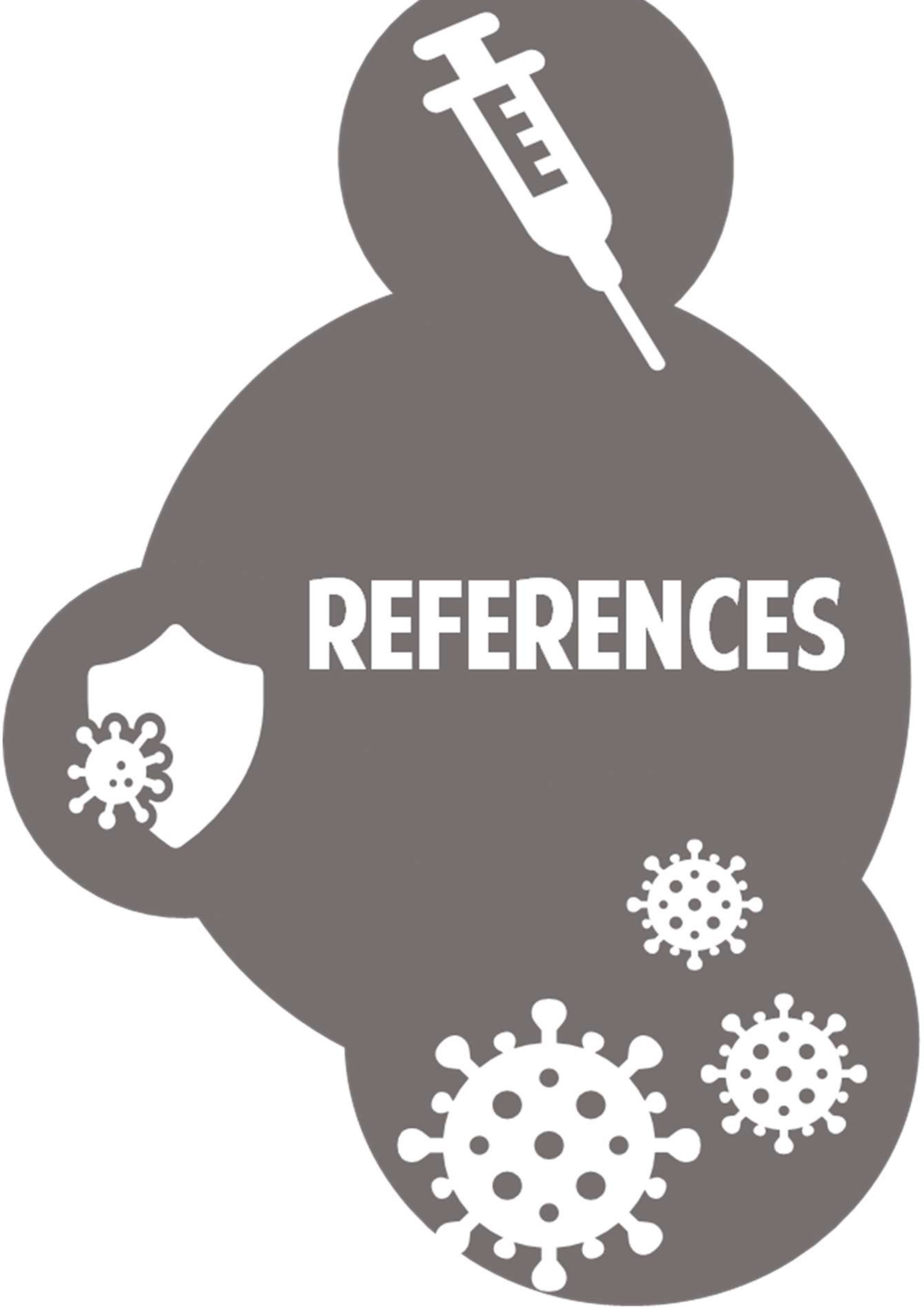
Conclusion

Based on the results from previous chapters, the main conclusions are as follows:

- The FMD outbreaks in Thailand have a seasonal pattern with the highest trend of FMD occurrence in October to November, which is the rainy to winter season. Thus, the routine vaccination should be done one month before October (Chapter 2).
- The spatial analysis shows the heterogenous distribution of the outbreaks. FMD outbreaks were mostly distributed in small clusters within a few subdistricts. Some high-risk areas with repeated outbreaks were detected in the central region of Thailand. Therefore, these areas should be prioritised for outbreak surveillance and control (Chapter 2).
- Risk factors related to FMD outbreaks included the increase in cattle and pig population, international border, livestock market and the occurrence of FMD outbreak in an adjacent area (Chapter 2).
- The morbidity and mortality rates of FMD varied across animal species, categories, and areas. The economic impact of FMD outbreaks at the farm level is considerable, particularly for dairy cattle and pig farms. In dairy farms, the average economic losses per cow was equivalent to roughly one-third of the farm's annual profit (Chapter 3).
- A spatial transmission kernel was used to quantify the between-farms transmission in this thesis. The transmission rate from the outbreak in

Thailand was higher than the transmission rate from FMD-free countries like the Netherlands and Japan. The larger farm size increased the susceptibility and infectivity of farms (Chapter 4).

- The outbreaks in the low-farm-density area were small even without intervention, and the implementation of control measures did not result in positive economic returns. On the contrary, in high-farm-density area, the outbreaks were big without intervention, and rigorous control measures were necessary for outbreak control. It highlights the need for customising control measures specific to the areas (Chapters 5 and 6).
- All control measures included in the model could limit the outbreak size and duration but resulted in different costs. Animal movement restrictions were exceptionally expensive and are not a practical option. Culling animals in the infected farms was the most effective measure for limiting the number of infected farms, , but it costed more than isolation of infected farms and ring vaccination. Ring vaccination was the cheapest control measure, given the similar effect of outbreak control (Chapter 6).
- Non-compliant farms were expected to have better benefits than compliant farms. Hence, farmers had a low monetary incentive to follow the measures. Control programs should include measures to incentivise farmers to comply to the measures (Chapter 6).



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SUMMARY

Summary

Summary

Foot and mouth disease (FMD) is a highly contagious viral disease that affects all cloven-hoofed animals, such as cattle, pigs, sheep, goats and buffaloes (Davies, 2002). It causes significant economic losses to the livestock industry due to production losses, trade restrictions, and the cost of implementing disease control measures (James et al., 2002; Knight-Jones et al., 2017; Knight-Jones & Rushton, 2013). FMD is in endemic in many regions of the world, such as Africa, Middle East and Asia, including Thailand (Brito et al., 2017). Although the Thai government is making efforts to prevent and control FMD, outbreaks still occur every year (WOAH, 2022a). This highlights the necessity of improving the control of FMD outbreaks, which requires obtaining information about the epidemiology and economics of FMD outbreaks. Therefore, the research questions of this thesis aim to gain information of the epidemiology and economics of FMD outbreaks and to evaluate FMD control measures by using bioeconomic modelling with this information. The research questions were broken down into 5 sub-objectives as follows:

I. Analyse the spatial and temporal pattern of the FMD outbreaks and investigate the risk factors associated with the FMD outbreak occurrence at the country level.
II. Assess the FMD epidemiological and economic impact at farm level.
III. Study the transmission dynamic of FMD outbreak in the endemic area of Thailand.
IV. Develop the FMD transmission model based on the inputs from real outbreaks and use this model to evaluate the consequences of control measures in different area conditions.
V. Evaluate the economic consequences of control measures by the integrated epidemiological and economic model.

In Chapter 2, epidemiology of FMD outbreaks at national level were studied using the national FMD outbreak data from 2011 to 2018. Multiple quantitative analyses were used for detecting temporal pattern, spatial pattern and risk factors of FMD outbreaks, including seasonal decomposition (Cleveland et al., 1990), Moran's I index (Assunção & Reis, 1999), mapping using standardised morbidity ratios (Waller & Gotway, 2004) and discrete Poisson scan statistics (Kulldorff, 2020), generalized estimating equation logistic regression models (GEE) (Halekoh et al., 2006). We found that the peak of annual FMD incidence was in October to November. The outbreaks were heterogeneously distributed

across the country with the detection of high-risk areas with repeated outbreaks in the central region. The risk factors related to FMD outbreaks included an increase in the cattle and pig population, international borders, livestock markets, and the occurrence of FMD outbreaks in adjacent areas. This study provides an overview of FMD outbreaks in Thailand and answers questions about when, where, and what the risk factors are for outbreaks. The results can help decision-makers allocate resources to high-risk areas and periods.

Chapter 3 studied the epidemiological and economic impacts at farm level. The interview data from FMD-affected farms from 4 districts of Thailand were used for analysis. The morbidity rate and mortality rate were calculated. We found that the morbidity and mortality rates of FMD varied across animal species, categories, and areas. In addition, the study calculated the economic impact of FMD on dairy farms. The largest economic losses resulted from decreased milk production. The estimated economic loss per cow was $56 USD on average, which is approximately equivalent to one-third of the animal's annual profit. These findings highlight the significant economic losses from FMD in dairy farms.

Chapter 4 studies transmission dynamics of FMD in subdistrict level using outbreak data from Lamphaya Klang subdistrict. A spatial transmission kernel, which is a function that describes how the between-farms transmission rate declines by the Euclidean between-farms distance (Boender et al., 2010), was applied to explain the between-farms transmission rate. From this function and data, the transmission parameters were derived using maximum likelihood estimation. The transmission rate from Thailand was higher compared to similar studies in the Netherlands (Boender et al., 2010) and Japan (Hayama et al., 2013). Moreover, the transmission rate significantly increased with the increase in farm size. These derived transmission parameters can serve as a basis for modelling FMD transmission in similar situations.

Chapter 5 and 6 were interrelated work on developing bioeconomic modelling to evaluate FMD control measures. In Chapter 5, the stochastic simulation model was developed to simulate FMD outbreaks at district level. This model relied on the concept of spatial transmission kernel to estimate the transmission rate between the farms (Boender et al., 2010). Moreover, the farm size (Boender et al., 2014), farm type (Backer et al., 2012), and animal trade network (Fajardo et al., 2021) were included in the model to reflect the diverse outbreaks that occur in different area settings. Multiple control measures were applied to simulation to assess the consequence, including culling all animals in the infected farms, ring vaccination, animal movement restriction and isolation of infected farms. From the simulation in low-farm-density area, FMD outbreaks were small, and the outbreak could end without any interventions. Thus, the effect of control measures in this area was not significant. In contrast, the outbreaks in the high-farm-density area were big without intervention. The outbreaks would continue until the susceptible farms in the area were depleted (Chapter 5). The difference of outbreaks between areas suggests that distinct control measures may be required for each of these areas.

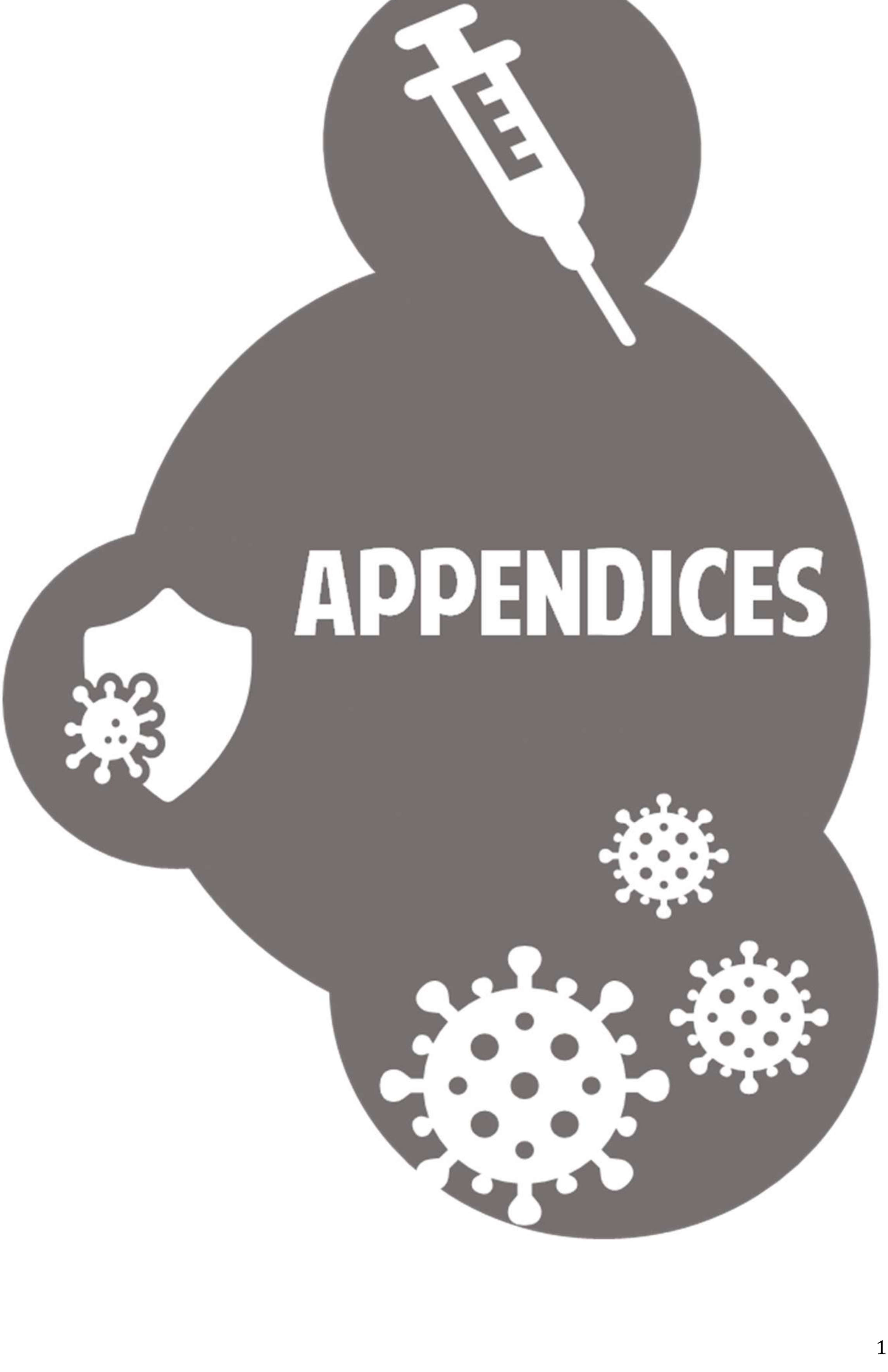
In Chapter 6, the model from Chapter 5 was extended to include economic analysis. Economic losses for different stakeholders, including government, non-compliant farmers, and compliant farmers, were calculated and compared across different scenarios. Furthermore, the effect of farmers' compliance on outbreak control was assessed. When comparing control measures in high-density farm areas, animal movement restrictions were found to be exceptionally expensive. Culling was the most effective control option for limiting the outbreak size and duration. However, its cost was higher compared to ring vaccination and isolation, despite the similar outcomes. Overall, ring vaccination was the cheapest option among all measures, given the similar outcomes of outbreak control. Each control measure resulted in different cost distributions among stakeholders. Non-compliant farms showed better financial results for all measures except ring vaccination when compared to compliant farms, indicating a significant financial motive for farmers to avoid complying with control measures. These results suggest that the government should customise control measures to specific areas and also focus on ensuring farmers' compliance.

Based on all finding, the main conclusion can be drawn as follows:

- The FMD outbreaks in Thailand have a seasonal pattern with the peak of FMD occurrences in October to November, which is the rainy to winter season. Thus, the routine vaccination should be done one month before October (Chapter 2).
- The spatial analysis shows the heterogenous distribution of the outbreaks. FMD outbreaks were mostly distributed in small clusters within a few adjacent subdistricts. Some high-risk areas with repeated outbreaks were detected in

the central region of Thailand. Therefore, these areas should be prioritised for outbreak surveillance and control (Chapter 2).

- Risk factors related to FMD outbreaks included the increase in cattle and pig population, international border, livestock market and the occurrence of FMD outbreak in an adjacent area (Chapter 2).
- The morbidity and mortality rates of FMD varied across animal species, categories, and areas. The economic impact of FMD outbreaks at the farm level was substantial, particularly for dairy cattle and pig farms. In dairy farms, the average economic loss per cow was equivalent to roughly one-third of the farm's annual profit (Chapter 3).
- The spatial transmission kernel was used to quantify the between-farms transmission in this thesis. The transmission from the outbreak in Thailand was higher than the transmission rate from FMD-free countries like the Netherlands and Japan. The larger farm size increased the susceptibility and infectivity of farms (Chapter 4).
- The outbreaks in the low-farm-density area were small even without intervention, and the implementation of control measures did not result in positive economic returns. On the contrary, in high-farm-density area, the outbreaks were big without intervention, and rigorous control measures were necessary for outbreak control. It highlights the need for customising control measures specific to the areas (Chapters 5 and 6).
- All control measures included in the model could limit the outbreak size and duration but resulted in different costs. Animal movement restrictions were exceptionally expensive and are not a practical option. Culling animals in the infected farms was the most effective measure for limiting the number of infected farms, but it costed more than isolation of infected farms and ring vaccination. Ring vaccination was the cheapest control measure, given the similar effect of outbreak control (Chapter 6).
- Non-compliant farms were expected to have better benefits than compliant farms. Hence, farmers had a low monetary incentive to follow the measures. Control programs should include measures to incentivise farmers to comply to the measures (Chapter 6).



APPENDICES

Appendices

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Thank you for everything :)

Wageningen, 2023

Thanicha Chanchaidechachai

About the author

Thanicha Chanchaidechachai (Ann) was born in Nakhon Pathom, Thailand on the 7th of January 1992. Since childhood, Thanicha has always been interested in animals and Biology. Therefore, she chose to study for a bachelor's degree in the faculty of Veterinary Medicine at Chulalongkorn University, Thailand. After graduation, she worked as a research assistant on foot and mouth (FMD) project in Thailand. During this period, she witnessed how farmers in Thailand struggled with animal diseases, especially FMD. For this reason, when she obtained a scholarship from Anandamahidol Foundation, she decided to pursue a Master's degree in Veterinary Epidemiology at Utrecht University, followed by a PhD in Animal Health Economics at Business Economics Group, Wageningen University & Research, focusing on FMD transmission and control measures in Thailand. She hopes that the findings from her studies will help understand FMD occurrences and improve disease control in Thailand. During her PhD, she also developed an interest in big data and improved her data science skills with side projects from several companies.

In her spare time, Thanicha enjoys hobbies such as gaming, drawing (as you can see her digital paintings in this thesis book), and cooking. She picked up several new hobbies during her time in the Netherlands, including fitness, where she enjoys strength training and lifting heavy weights as a way to relieve stress from her PhD. She also learned how to play the Irish tin whistle as her first musical instrument, even though she is still not good at it (yet). She can be reached by email at thanicha.c@outlook.co.th.

List of publications

Publications

- **Chanchaidechachai, T.**, de Jong, M. C. M., & Fischer, E. A. J. (2021). Spatial model of foot-and-mouth disease outbreak in an endemic area of Thailand. Preventive Veterinary Medicine, 195(March), 105468. https://doi.org/10.1016/j.prevetmed.2021.105468
- **Chanchaidechachai, T.**, Saatkamp, H., Inchaisri, C., & Hogeveen, H. (2022). Analysis of Epidemiological and Economic Impact of Foot-and-Mouth Disease Outbreaks in Four District Areas in Thailand. Frontiers in Veterinary Science, 9(June), 1–8. https://doi.org/10.3389/fvets.2022.904630
- **Chanchaidechachai, T.**, Saatkamp, H., de Jong, M., Inchaisri, C., Hogeveen, H., Premashthira, S., Buamitoup, N., Prakotcheo, R., & van den Borne, B. H. P. (2022). Epidemiology of foot - and - mouth disease outbreaks in Thailand from 2011 to 2018. Transboundary and Emerging Diseases, 69(6), 3823–3836. https://doi.org/10.1111/tbed.14754
- **Chanchaidechachai, T.**, Saatkamp, H.W., Hogeveen, H., de Jong, M.C.M., Fischer, E.A.J., 2023. Evaluation of Foot-and-Mouth Disease control measures in endemic areas of Thailand, in: Brodbelt, D., van Schaik, G. (Eds.), Society for Veterinary Epidemiology and Preventive Medicine, Proceedings: Toulouse, France, 22-24 March 2023 (SVEPM Proceedings) . pp. 83–96.
- **Chanchaidechachai, T.**, Saatkamp, H., Hogeveen, H., de Jong, M. C. M., & Fischer, E. A. J. Evaluation of foot and mouth disease control measures: Simulating two endemic areas of Thailand (submitted)

Conferences

- **Oral presentation: Chanchaidechachai, T.**, Saatkamp, H., de Jong, M. C. M., Fischer, E. A. J. & Hogeveen, H. (2023) Assessment of area-specific control of FMD in Thailand with a bioeconomic model. ISESSAH conference. Helsinki, Finland. 13 – 15 June 2023.

Thanicha Chanchaidechachai

Wageningen School of Social Sciences (WASS) Completed Training and Supervision Plan

Name of the learning activity	Department/Institute	Year	ECTS*
Project related competences			
A1 Managing a research project			
WASS introduction course	WASS	2020	1
“Epidemiological Impacts of FMD Outbreaks at Farm Level in 4 Outbreak Areas of Thailand and Economic Assessment in Dairy Farms”	ISESSAH	2021	1
PhD meetings BEC	BEC	2020-2023	2
Scientific Writing	Wageningen in’to Languages	2021	1.8
Project and time management	WGS	2020	1.5
Writing research proposal	WUR	2020	6
A2 Integrating research in the corresponding discipline			
Big Data Analysis in the Life Sciences	VLAG	2021	0.9
Systematic Literature Review	WASS	2021	4
Multivariate Data Analysis, YRM 50806	WUR	2021	6
Introduction to programming in R for social sciences	WASS	2022	3
General research related competences			
B1 Placing research in a broader scientific context			
Advanced Statistics course Design of Experiments	WIAS	2022	0.8
Introduction to Zero inflated model with R	PE&RC	2021	1.5
Intermediate programming in R	PE&RC	2022	1.2
R and Big Data	PE&RC	2021	0.6
Tidy data transformation and visualization with R	PE&RC	2021	1.2
Statistical uncertainty analysis of dynamic models	PE&RC	2022	1.5
Advanced Statistics course Design of Experiments	WIAS	2022	0.8
B2 Placing research in a societal context			
Organize the online seminars for Thai student association in the Netherlands for the topic of “Presentation technique” and “Handle stress for your success”	Thai student association in the Netherlands (TSAN)	2022	2
Career related competences/personal development			
C1 Employing transferable skills in different domains/careers			
Writing grant proposal	Wageningen in’to Languages	2022	1.6
Total			37.6

*One credit according to ECTS is on average equivalent to 28 hours of study load

Colophon

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